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L84  ANSWER 1 OF 29  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:844214  HCAPLUS
DN   142:54873
ED   Entered STN:  15 Oct 2004
TI   Preparation of β-1,3-glucan from Ganoderma lucidum
IN   Lee, Shin Young; Kang, Tae Soo
PA   Lee, Shin-Young, S. Korea
SO   Repub. Korea, No pp. given
     CODEN: KRXXFC
DT   Patent
LA   Korean
IC   ICM  C12P019-04
CC   16-4 (Fermentation and Bioindustrial Chemistry)
FAN.CNT 1
     PATENT NO.          KIND   DATE       APPLICATION NO.         DATE
     ---------------     ----   --------   --------------------    --------
PI   KR 156986           B1     19981015   KR 1995-3283            19950220 <--
PRAI KR 1995-3283                 19950220  <--
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
 --------------   -----  ----------------------------------------------
 KR 156986        ICM    C12P019-04
AB   A production method of polysaccharides from liquid culture of Ganoderma
lucidum,
     which is secreted in the medium and collected from culture broth is
     provided.  Ganoderma lucidum is cultured to produce β-1,3-glucan
     under optimal culture conditions such as a ratio of C/N being 7-9.5:1, pH
     4.0-6.0. and 80-140 rpm of stirring speed, by liquid culture.  The culture
     medium is consisted 3-10 % of glucose, 0.1-1.0 % of yeast extract, 0.05-0.3 %
     of ammonium hydrogen phosphate and 0.05-0.3 % of potassium phosphate.
     Soluble starch, mannose, lactose and maltose can be used as a carbon source
     and malts extract, ammonium sulfate and ammonium chloride as a nitrogen
     source.  Flask culture, batch, fed batch and continuous culture are used
     to produce polysaccharides.  Potato dextrose agar (PDA) is used to keep
     the fungi grown at 37 °C for 7 days after then 4 .
     degree.C.  Seed culture is carried out 100 mL flask with 4-5 disks
     taken from PDA plate at 30 °C for 7 days.  The main
     culture is done with 250 mL flask inoculated with 5 volume % of seed
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culture. The polysaccharides secreted in the medium are collected by ultrafiltration, acetone precipitated and freeze dried.
ST Ganoderma exopolysaccharide fermn
IT **Fermentation**
(batch; preparation of β-1,3-glucan from Ganoderma lucidum)
IT **Fermentation**
(**continuous**; preparation of β-1,3-glucan from Ganoderma lucidum)
IT Polysaccharides, preparation
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(exopolysaccharides; preparation of β-1,3-glucan from Ganoderma lucidum)
IT **Fermentation**
(fed-batch; preparation of β-1,3-glucan from Ganoderma lucidum)
IT Carbon sources, microbial
Culture media
Freeze drying
Ganoderma lucidum
Nitrogen sources, microbial
Precipitation (chemical)
Ultrafiltration
(preparation of β-1,3-glucan from Ganoderma lucidum)
IT 63-42-3, Lactose 69-79-4, Maltose 3458-28-4, D-Mannose 7783-20-2, Ammonium sulfate, processes 9005-25-8, Starch, processes 12125-02-9, Ammonium chloride, processes
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(preparation of β-1,3-glucan from Ganoderma lucidum)
IT 9051-97-2P, 1,3-β-Glucan
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(preparation of β-1,3-glucan from Ganoderma lucidum)
IT 67-64-1, Acetone, processes
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PROC (Process)
(preparation of β-1,3-glucan from Ganoderma lucidum)

L84 ANSWER 2 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2004:470353** HCAPLUS
DN **141:5893**
ED Entered STN: 10 Jun 2004
TI Enzymic acylation of flavonoids
IN Moussou, Philippe; Falcimaigne, Aude; Pauly, Gilles; Ghoul, Mohamed; Engasser, Jean-Marc; Ardhaoui, Melika
PA Cognis France S.A., Fr.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA German
IC ICM C12P007-62
ICS C12P017-06
CC 16-5 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 7, 26
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1426445	A1	20040609	EP 2002-292969	20021203 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2004050889	A2	20040617	WO 2003-EP13143	20031122 <--
WO 2004050889	A3	20040812		
W: JP, KR, US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

IT, LU, MC, NL, PT, RO, SE, SI, SK, TR
PRAI EP 2002-292969 A 20021203 <--
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 1426445	ICM	C12P007-62
	ICS	C12P017-06
EP 1426445	ECLA	C12P007/62; C12P017/06 <--

AB A process is provided for the enzymic acylation of glycosylated flavonoids. Thus, rutin was acylated with palmitic acid by the immobilized lipase Novozyme 435 ® in a tert-amyl alc. solvent system. The reaction was conducted at 60 °C under vacuum (150 mbar). Water was removed from the gas phase by a mol. sieve. After 48 h reaction time, 90% of the substrates were consumed. The enzyme was removed by filtration, and unreacted substrates were removed by solvent extraction

ST enzymic acylation flavonoid

IT Binary systems
(aqueous two-phase; enzymic acylation of flavonoids)

IT Enzymes, uses
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(com.; enzymic acylation of flavonoids)

IT Adsorption
Crystallization
Distillation
Liquid chromatography
Molecular sieves
Partial pressure
Pervaporation
Precipitation (chemical)
(enzymic acylation of flavonoids)

IT Anthocyanins
Flavonoids
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(enzymic acylation of flavonoids)

IT Acylation
Esterification
(enzymic; enzymic acylation of flavonoids)

IT Bioreactors
(flow; enzymic acylation of flavonoids)

IT Enzymes, uses
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(immobilized; enzymic acylation of flavonoids)

IT **Temperature**
(of reaction; enzymic acylation of flavonoids)

IT Extraction
(supercrit.; enzymic acylation of flavonoids)

IT 9001-62-1, Lipase 9001-92-7, Protease
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(enzymic acylation of flavonoids)

IT 67-63-0, 2-Propanol, processes 67-64-1, Acetone, processes 75-05-8, Acetonitrile, processes 75-65-0, tert-Butanol, processes 75-85-4, 2-Methyl-2-butanol 78-83-1, Isobutanol, processes 78-92-2, 2-Butanol 78-93-3, Butanone, processes 107-21-1, 1,2-Ethanediol, processes 107-87-9, 2-Pentanone 110-54-3, Hexane, processes 123-91-1, Dioxane, processes 142-82-5, Heptane, processes 513-85-9, 2,3-Butanediol 66309-84-0, 4-Hydroxy-2-methylpentanone
RL: BCP (Biochemical process); CPS (Chemical process); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)

(enzymic acylation of flavonoids)
IT 57-10-3D, Palmitic acid, derivs. and/or Me, Et, Pr, or Bu esters of 65-85-0D, Benzoic acid, derivs. and/or Me, Et, Pr, or Bu esters of 90-47-1D, Xanthone, and derivs. 91-64-5D, Coumarin, and derivs. 94-41-7D, Chalcone, and derivs. 99-50-3D, Protocatechuic acid, derivs. and/or Me, Et, Pr, or Bu esters of 106-14-9D, 12-Hydroxyoctadecanoic acid, derivs. and/or Me, Et, Pr, or Bu esters of 117-39-5, Quercetin 121-34-6D, Vanillic acid, derivs. and/or Me, Et, Pr, or Bu esters of 123-99-9D, Azelaic acid, derivs. and/or Me, Et, Pr, or Bu esters of 149-91-7D, Gallic acid, derivs. and/or Me, Et, Pr, or Bu esters of 153-18-4, Rutin 331-39-5D, Caffeic acid, derivs. and/or Me, Et, Pr, or Bu esters of 487-26-3D, Flavanone, and derivs. 505-54-4D, Hexadecanedioic acid, derivs. and/or Me, Et, Pr, or Bu esters of 506-13-8D, 16-Hydroxyhexadecanoic acid, derivs. and/or Me, Et, Pr, or Bu esters of 520-26-3, Hesperidin 525-82-6D, Flavone, and derivs. 531-75-9, Esculin 574-12-9D, Isoflavone, and derivs. 577-85-5D, Flavonol, and derivs. 621-82-9D, Cinnamic acid, derivs. and/or Me, Et, Pr, or Bu esters of 1135-24-6D, Ferulic acid, derivs. and/or Me, Et, Pr, or Bu esters of 7530-92-9D, Thiooctanoic acid, derivs. and/or Me, Et, Pr, or Bu esters of 25429-38-3D, Coumaric acid, derivs. and/or Me, Et, Pr, or Bu esters of 27215-73-2D, Flavanol, and derivs. 36413-60-2D, Quinic acid, derivs. and/or Me, Et, Pr, or Bu esters of 71310-21-9D, 11-Mercaptoundecanoic acid, derivs. and/or Me, Et, Pr, or Bu esters of
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(enzymic acylation of flavonoids)
IT 697298-96-7P
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(enzymic acylation of flavonoids)
IT 697298-93-4P 697298-94-5P 697298-95-6P
RL: BMF (Bioindustrial manufacture); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(enzymic acylation of flavonoids)
IT 7732-18-5P, Water, preparation
RL: BYP (Byproduct); REM (Removal or disposal); PREP (Preparation); PROC (Process)
(enzymic acylation of flavonoids)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anne-Marie, M; US 6235294 B1 2001 HCAPLUS
(2) Danieli; HELVETICA CHIMICA ACTA 1990, 7, HCAPLUS
(3) Gao, C; BIOTECHNOLOGY AND BIOENGINEERING - COMBINATORIAL CHEMISTRY 2001, 3
(4) Henkel Kgaa; WO 0179245 A 2001 HCAPLUS

L84 ANSWER 3 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:468027 HCAPLUS
DN 141:22295
ED Entered STN: 10 Jun 2004
TI Process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments
IN **Markussen, Jan; Diers, Ivan**
PA **Novo Nordisk** A/S, Den.
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12P021-00
ICS C07K001-14
CC 16-2 (**Fermentation** and Bioindustrial Chemistry)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2004048588 A1 20040610 WO 2003-DK801 20031124 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004137571 A1 20040715 US 2003-719601 20031121 <--
PRAI DK 2002-1821 A 20021126 <--
US 2002-430748P P 20021204 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004048588	ICM	C12P021-00
	ICS	C07K001-14

AB A process is provided for purifying a fermentation-derived product comprising: **heating** fermentation broth containing the fermentation-derived product or a precursor to a **temperature** greater than **60** **.degree**.C; **cooling** the fermentation broth to a **temperature** below **60** °C; separating the precipitated materials from the soluble portion of the fermentation broth at a **temperature** less than **60** **degree**.C; and isolating the fermentation-derived product using microfiltration, ultrafiltration, or liquid chromatog. The process thus removes impurities in the fermentation by precipitation prior to membrane or column chromatog. and hence lessens the possibility of fouling occurring in these process steps due to uncontrolled precipitation Thus, recombinant Saccharomyces cerevisiae fermentation broth the single chain **insulin** analog SCI-13, was harvested and clarified by centrifugation. Then ethanol was added to the centrifugate at a 3:2 ratio and the pH was adjusted to 3.0. The precipitate which formed was removed by centrifugation and the supernatant was then subjected to 5 min **heat** treatments at **60**, 80, and 93 **degree**.C resp. Anal. of the **heat** treated supernatant showed that impurities were precipitated and that the SCI-13 **peptide** was fully solubilized by the **heat** treatment.

ST fermn broth recombinant **insulin** analog **heat** treatment

IT **Peptides**, preparation
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(**TFF**, precursors and analogs of; process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)

IT **Fermentation**
(**broth**; process for purifying recombinant **insulin** analogs from fermentation **broth** using **heat** treatments)

IT Residence time
(for **heat** treatment; process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)

IT Preparative liquid chromatography
(high-performance reversed-phase; process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)

IT Filtration
(microfiltration; process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)

IT **Albumins, preparation**

Interleukins
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(precursors and analogs of; process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)
IT Reversed phase HPLC
(preparative; process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)
IT Centrifugation
Fouling
Heat treatment
Liquid chromatography
Precipitation (chemical)
Temperature
Ultrafiltration
(process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)
IT **Solubilization**
(**protein**; process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)
IT Candida utilis
Escherichia coli
Kluyveromyces lactis
Pichia methanolica
Pichia pastoris
Saccharomyces cerevisiae
(suitable recombinant host; process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)
IT **9004-10-8DP**, **Insulin**, precursors and analogs of
9007-92-5DP, **Glucagon**, precursors and analogs of
89750-14-1DP, **GLP-1**, precursors and analogs of
89750-15-2DP, **Glucagon**-like **peptide** II, precursors and analogs of **130391-54-7DP**, **Exendin**-3, precursors and analogs of **141732-76-5DP**, **Exendin**-4, precursors and analogs of **204521-68-6P 698973-76-1P 698973-77-2P**, SCI 13
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)
IT 64-17-5, Ethanol, processes
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PROC (Process)
(process for purifying recombinant **insulin** analogs from fermentation broth using **heat** treatments)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; PATENT ABSTRACTS OF JAPAN 1998, V1998(09)
(2) Basf Ag; EP 0438767 A 1991 HCAPLUS
(3) Genex Corp; WO 9000200 A 1990 HCAPLUS
(4) Green Cross Corp; EP 0699687 A 1996 HCAPLUS
(5) Juridical Foundation; EP 1329462 A 2003 HCAPLUS
(6) Merck & Co Inc; EP 0431679 A 1991 HCAPLUS
(7) Pearce, R; US 5455331 A 1995 HCAPLUS
(8) Shinotesuto Kk; JP 10101696 A 1998 HCAPLUS

L84 ANSWER 4 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:976858 HCAPLUS
DN 140:27153
ED Entered STN: 15 Dec 2003
TI **Heating** and acidifying precipitation process for producing plant

leaf **protein**
IN Qin, Heyuan
PA Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 4 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
IC ICM A23J003-14
ICS A23J003-32
CC 17-14 (Food and Feed Chemistry)
Section cross-reference(s): 9, **16**
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1348702	A	20020515	CN 2000-126635	20001016 <--
	CN 1127907	B	20031119		
PRAI	CN 2000-126635		20001016 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
CN 1348702	ICM	A23J003-14
	ICS	A23J003-32

AB The title process comprises beating plant, pressing, and precipitating; and is characterized in **heating** the plant juice to 80-100.
degree., **cooling** to **40**-50°,
before the precipitation with lactic acid fermentation broth. The process is low in
precipitation time.
ST leaf **protein heating** acidification pptn prepn
IT **Fermentation**
(**broth**; **heating** and acidifying precipitation process for producing edible plant leaf **protein**)
IT **Heating**
Precipitation (chemical)
Sterilization and Disinfection
pH
(**heating** and acidifying precipitation process for producing edible plant leaf **protein**)
IT **Proteins**
RL: FFD (Food or feed use); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**heating** and acidifying precipitation process for producing edible plant leaf **protein**)
IT Leaf
(plant; **heating** and acidifying precipitation process for producing edible plant leaf **protein**)
IT 50-21-5, Lactic acid, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**heating** and acidifying precipitation process for producing edible plant leaf **protein**)

L84 ANSWER 5 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2003:882856** HCAPLUS
DN **139:349732**
ED Entered STN: 11 Nov 2003
TI Mild soluble collagen enzymic manufacture from pig skin
IN Jang, Bu-sik; Kim, Tae-Yeong
PA Boowon Biotech Co., Ltd., S. Korea
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese

IC ICM C12P021-06
ICS C12S007-00
CC 16-5 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 17
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2003319794	A2	20031111	JP 2002-354015	20021205 <--
	KR 2002044115	A	20020614	KR 2002-23965	20020501 <--
PRAI	KR 2002-23965	A	20020501 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 2003319794	ICM	C12P021-06
	ICS	C12S007-00

AB The mild soluble collagen (I) (mol.-weight, 1000-2000) is manufactured from pig skin
by chopping, first enzymic reaction with protease of Bacillus licheniformis at pH 6.5-8.5 and 55-70°, second enzymic reaction with protease of B. amyloliquefaciens at pH 5.5-7.5 and 45-55. **degree.**, vacuum concentration, sterilization, and drying. The method does not require processes such as pre-treatment with acid, washing, etc. It is low in cost, and the product is free of acid and other heavy metals. I is useful for manufacturing health food and **protein** supplement.
ST collagen soly manuf protease Bacillus pig skin
IT Hydrolysis
(enzymic; mild soluble collagen enzymic manufacture from pig skin)
IT Bacillus amyloliquefaciens
Bacillus licheniformis
Fermentation
Food solubility
Health food
Temperature effects, biological
pH
(mild soluble collagen enzymic manufacture from pig skin)
IT Skin
(pig; mild soluble collagen enzymic manufacture from pig skin)
IT **Proteins**
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(supplements; mild soluble collagen enzymic manufacture from pig skin)
IT 9001-92-7, Protease
RL: CAT (Catalyst use); USES (Uses)
(mild soluble collagen enzymic manufacture from pig skin)

L84 ANSWER 6 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2003:796239** HCAPLUS
DN **139:291126**
ED Entered STN: 10 Oct 2003
TI Control of glycoforms in IgG
IN Devries, Ruth L.; Vickroy, Thomas Bruce
PA USA
SO U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM C12P021-04
NCL 435070210
CC 15-3 (Immunochemistry)
Section cross-reference(s): **16**
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003190710	A1	20031009	US 2002-109117	20020328 <--

US 2004214289 A1 20041028 US 2004-848421 20040518 <--
PRAI US 2002-109117 A3 20020328 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003190710	ICM	C12P021-04
	NCL	435070210
US 2004214289	ECLA	C07K016/00 <--

AB The disclosed invention provides a method to control the levels of IgG non-glycosylated heavy chains (NGHC) in a CHO cell culture process producing a recombinant monoclonal antibody. By adjusting the cell culture **temperature**, the batched medium osmolality, or both, of a cell culture such as a production culture, the levels of NGHC can be decreased or increased. Batched medium osmolality of a final seed culture used to inoculate a production culture can optionally be adjusted to match that of the production culture. The authors describe a proprietary medium consisting of a basal formulation containing amino acids, salts, trace elements, and vitamins similar to those described in PCT International Publication Number WO 92/05246.

ST nonglycosylated IgG heavy chain cell culture **temp** medium osmolality

IT Named reagents and solutions
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(CD-CHO; IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality)

IT Animal cell line
(CHO; IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality)

IT Named reagents and solutions
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(EX-CELL 325; IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality)

IT Culture media
Osmolality
Temperature effects, biological
(IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality)

IT Bioreactors
(IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality in)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG; IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heavy chain, non-glycosylated (NGHC); IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality)

IT Yeast
(hydrolyzate; IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality in proprietary media containing)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(mixture; IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality in proprietary media containing)

IT 59-05-2, Methotrexate 144-55-8, Sodium bicarbonate, biological studies 497-19-8, Sodium carbonate, biological studies 7447-40-7, Potassium chloride (KCl), biological studies 7647-14-5, Sodium chloride, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality in proprietary media containing)

IT 50-99-7, Glucose, biological studies 12286-76-9, Ferric fructose 17099-81-9, Ferric EDTA
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality in proprietary media containing)

IT **9004-10-8, Insulin**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(recombinant; IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality in proprietary media containing)

IT 106392-12-5, Lutrol F68
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(surfactant; IgG non-glycosylated heavy chain levels regulation in CHO cell culture by adjusting cell culture **temperature** and/or batched medium osmolality in proprietary media containing)

L84 ANSWER 7 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2003:40004** HCAPLUS
DN **138:286042**
ED Entered STN: 17 Jan 2003
TI Optimisation of the solubility of the recombinant Itk kinase domain in Escherichia coli
AU Meinander, Nina Q.; Jeppsson, Marie; Sogaard, Morten
CS Mol. Sci., AstraZeneca Lund R&D, Lund, S-22187, Swed.
SO Recombinant Protein Production with Prokaryotic and Eukaryotic Cells: A Comparative View on Host Physiology, Selected Articles from the Meeting of the EFB Section on Microbial Physiology, Semmering, Austria, Oct. 5-8, 2000 (**2001**), Meeting Date 2000, 159-170. Editor(s): Merten, Otto-Wilhelm. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.
CODEN: 69DLJQ; ISBN: 0-7923-7137-2
DT Conference
LA English
CC 16-1 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 3
AB The effect of fermentation **temperature**, inducer concentration and overexpression of GroEL/S chaperones or thioredoxin on the solubility of GST-ItkKD expressed in E. coli was investigated. The solubilities of two slightly different GST-ItkKD constructs, of which one had a 12 amino acid-residue shorter kinase domain than the other, were compared. The GST-tag of the shorter construct was replaced with an MBP-tag, and the solubilizing effect of the tags was compared. Decreasing the fermentation **temperature** from 37. **degree**.C to 20°C doubled the soluble **protein** expression of the shorter kinase domain construct. Coexpression of the GroEL/S chaperones resulted in minor (1.5-2.5-fold) improvements in the solubility of both constructs, while coexpression of TRX or decreasing the IPTG concentration had very little effect. The longer kinase domain construct was around 5 times more soluble than the shorter. The greatest effect on solubility

was achieved by changing the tag from GST to MBP, yielding a tenfold increase in solubility

ST Escherichia recombinant Itk kinase domain soly fusion **protein**

IT Molecular chaperones
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(GroEL; optimization of solubility of recombinant Itk kinase domain in Escherichia coli)

IT Molecular chaperones
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(GroES; optimization of solubility of recombinant Itk kinase domain in Escherichia coli)

IT **Proteins**
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(MBP (maltose-binding **protein**), fusion **protein** with itk kinase; optimization of solubility of recombinant Itk kinase domain in Escherichia coli)

IT Affinity chromatography
Genetic engineering
Solubility
Temperature effects, biological
(optimization of solubility of recombinant Itk kinase domain in Escherichia coli)

IT Thioredoxins
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(optimization of solubility of recombinant Itk kinase domain in Escherichia coli)

IT Fusion **proteins** (chimeric **proteins**)
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(optimization of solubility of recombinant Itk kinase domain in Escherichia coli)

IT Escherichia coli
(recombinant; optimization of solubility of recombinant Itk kinase domain in Escherichia coli)

IT 367-93-1, IPTG
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(optimization of solubility of recombinant Itk kinase domain in Escherichia coli)

IT 50812-37-8DP, Glutathione-S-transferase, fusion **protein** with itk kinase 151662-26-9DP, fusion **protein** with glutathione-S-transferase or maltose binding **protein**
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(optimization of solubility of recombinant Itk kinase domain in Escherichia coli)

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L84 ANSWER 8 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2002:966511** HCAPLUS
DN **138:88734**
ED Entered STN: 22 Dec 2002
TI Effect of **temperature** on the growth of recombinant E. coli and on the expression of recombinant **protein**
AU Ye, Jiao; Chen, Chang-hua; Xia, Jie; Fu, Shui-lin; Yang, Ya-qin
CS State Key Laboratory of Bioreactor Engineering ECUST, Shanghai, 200237, Peop. Rep. China
SO Huadong Ligong Daxue Xuebao (**2002**), 28(4), 364-367
CODEN: HLIXEV; ISSN: 1006-3080
PB Huadong Ligong Daxue Xuebao Bianjibu
DT Journal
LA Chinese
CC 16-5 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 10
AB The expression of rhCu/Zn-SOD in recombinant E. coli BL21 (DE3) at different induction **temps.** was investigated. The growth of E. coli and the expression of the recombinant **protein** were studied and compared at 37° or 30°. The recombinant E. coli was cultivated in 5L fermentor, results of which showed that at 30° the specific growth rate was reduced while the viability of recombinant E. coli and plasmid stability were greatly increased. The stability and solubility of the recombinant **protein** were also improved. The maximum enzyme activity of rhCu/Zn-SOD expressed at 30° was increased to 4 757 U/mL, which was 2.7 times as that at 37°.
ST Escherichia recombinant manuf **protein temp**; superoxide dismutase recombinant manuf Escherichia **temp**
IT Escherichia coli
Fermentation
Growth, microbial
Solubility
Temperature effects, biological
(effect of **temperature** on growth of recombinant E. coli and on expression of recombinant **protein**)
IT Plasmids
(stability; effect of **temperature** on growth of recombinant E. coli and on expression of recombinant **protein**)
IT 9054-89-1P, Superoxide dismutase
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(Zinc; effect of **temperature** on growth of recombinant E. coli and on expression of recombinant **protein**)

L84 ANSWER 9 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2002:927610** HCAPLUS
DN **137:383889**
ED Entered STN: 06 Dec 2002
TI Enzymatic synthesis α-glucans
IN Fujii, Kazutoshi; Terada, Yoshinobu; Yanase, Michiyo; Odan, Koji; Takata, Hiroki; Takaha, Takeshi; Kuriki, Takashi; Okada, Shigetaka
PA Ezaki Glico Co., Ltd., Japan
SO PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12P019-04

ICS C08B015-00; C08B030-00
CC 16-2 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 33
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002097107	A1	20021205	WO 2002-JP5125	20020527 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1390520	A1	20040225	EP 2002-774073	20020527 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004526463	T2	20040902	JP 2003-500272	20020527 <--
	US 2004115778	A1	20040617	US 2003-475943	20031024 <--
PRAI	JP 2001-159744	A	20010528 <--		
	WO 2002-JP5125	W	20020527 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002097107	ICM	C12P019-04
	ICS	C08B015-00; C08B030-00
JP 2004526463	FTERM	4B064/AF12; 4B064/CA21; 4B064/CB30; 4B064/CC03; 4B064/CC06; 4B064/CC09; 4B064/CC24; 4B064/CD01; 4B064/CD09; 4B064/CD15; 4B064/CD19; 4B064/CE06; 4B064/CE10; 4B064/CE15; 4B064/DA10; 4B064/DA16 <--

AB A first method for producing glucan comprises the step of allowing a reaction solution containing sucrose, a primer, inorg. phosphate or glucose-1-phosphate, sucrose phosphorylase, and glucan phosphorylase to react to produce glucans. The maximum value of the sucrose-phosphate ratio of the reaction solution from the start of the reaction to the end of the reaction is no more than about 17. A second method for producing glucan comprises the step of allowing a reaction solution containing sucrose, a primer, inorg. phosphate or glucose-1-phosphate, sucrose phosphorylase, and glucan phosphorylase to react to produce glucans. The reaction is conducted at a **temperature** of about 40 °C to about 70 **.degree** .C. Thus, when a mixture containing 8% sucrose, 4 mM maltoheptaose, 40 mM inorg. phosphate and 10 U/g Streptococcus mutans sucrose phosphorylase and 10 U/g Thermus aquaticus glucan phosphorylase were reacted at 50 . **degree**.C, the amylose yield was 100% based on sucrose.

ST enzymic biosynthesis amylose alpha glucan
IT Genetic engineering
Molecular cloning
(enzymic synthesis α-glucans)
IT Maltooligosaccharides
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(enzymic synthesis α-glucans)
IT Hydrolysis
Polymerization
(enzymic; enzymic synthesis α-glucans)
IT **Precipitation (chemical)**
(for enzyme recovery; enzymic synthesis α-glucans)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(for glucan phosphorylase; enzymic synthesis α-glucans)
IT **Temperature**
(for reaction; enzymic synthesis α-glucans)
IT Gene, microbial
Gene, plant
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for sucrose phosphorylase; enzymic synthesis α-glucans)
IT Bacillus stearothermophilus
Solanum tuberosum
Thermus aquaticus
(glucan phosphorylase source; enzymic synthesis α-glucans)
IT Enzymes, uses
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(immobilized; enzymic synthesis α-glucans)
IT Separation
(liquid-solid, to recover α-glucans; enzymic synthesis α-glucans)
IT Concentration (condition)
(of sucrose, effects on amylose yield; enzymic synthesis α-glucans)
IT **Thermal** stability
(of various enzyme catalytic mixts.; enzymic synthesis α-glucans)
IT **Temperature effects, biological**
(on α-glucan formation; enzymic synthesis α-glucans)
IT Escherichia coli
(recombinant, for enzyme production; enzymic synthesis α-glucans)
IT Aquifex aeolicus
(source of debranching enzyme; enzymic synthesis α-glucans)
IT Granulicatella adiacens
Streptococcus mutans
Streptococcus pneumoniae
Streptococcus thermophilus
(sucrose phosphorylase source; enzymic synthesis α-glucans)
IT Ultrafiltration
(to purify α-glucans; enzymic synthesis α-glucans)
IT 9005-82-7P, Amylose
RL: BCP (Biochemical process); BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(enzymic synthesis α-glucans)
IT 9035-74-9P, Glucan phosphorylase 9074-06-0P, Sucrose phosphorylase
RL: BCP (Biochemical process); BPN (Biosynthetic preparation); CAT (Catalyst use); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(enzymic synthesis α-glucans)
IT 57-48-7P, D-Fructose, preparation
RL: BCP (Biochemical process); BYP (Byproduct); RCT (Reactant); REM (Removal or disposal); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(enzymic synthesis α-glucans)
IT 9001-97-2 9012-47-9, E.C. 3.2.1.33 9032-09-1 9067-73-6 9075-68-7, Pullulanase
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(enzymic synthesis α-glucans)
IT 50-99-7, Dextrose, reactions 59-56-3 69-79-4, Maltose 1109-28-0, Maltotriose 7558-79-4, Disodium phosphate 7778-77-0, Monopotassium phosphate 9004-53-9, Dextrin 9005-25-8D, Starch, and derivs. 9005-79-2, Glycogen, reactions 9037-22-3, Amylopectin 9057-02-7, Pullulan 14265-44-2, Phosphate, reactions 34620-78-5, Maltoheptaose 167679-07-4, Tetrup H

RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(enzymic synthesis α-glucans)
IT 9074-78-6P, α-Glucan
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(enzymic synthesis α-glucans)
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L84 ANSWER 10 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2002:807710** HCAPLUS
DN **138:33466**
ED Entered STN: 24 Oct 2002
TI True and Apparent **Temperature** Dependence of **Protein** Adsorption Equilibrium in Reversed-Phase HPLC
AU Szabelski, Pawel; Cavazzini, Alberto; Kaczmarski, Krzysztof; Van Horn, Jennifer; Guiochon, Georges
CS Department of Chemistry, The University of Tennessee, Knoxville, TN, 37996-1600, USA
SO Biotechnology Progress (**2002**), 18(6), 1306-1317
CODEN: BIPRET; ISSN: 8756-7938
PB American Chemical Society
DT Journal
LA English
CC 2-1 (Mammalian Hormones)
Section cross-reference(s): 9, **16**
AB The adsorption behavior of bovine **insulin** on a C8-bonded silica stationary phase was investigated at different column pressures and **temps.** in isocratic reversed-phase HPLC. Changes in the molar volume of **insulin** (ΔVm) upon adsorption were derived from the pressure dependence of the isothermal retention factor (k'). The values of ΔVm were found to be practically independent of the **temperature** between 25 and 50° at -96 mL/mol and to increase with increasing **temperature**, up to -108 mL/mol reached at 50. **degree.**. This trend was confirmed by two sep. series of measurements of the **thermal** dependence of ln(k'). In the first series the average column pressure was kept constant The second series involved measurements of ln(k') under constant mobile-phase flow rate, the average column pressure varying with the **temperature** In both cases, a parabolic shape relationship was observed between ln(k') and the **temperature**, but the values obtained for ln k' were higher in the first than in the second case. The relative difference in ln(k'), caused by the change in pressure drop induced by the **temperature**, is equivalent to a systematic error in the estimate of the Gibbs free energy of 12%. Thus, a substantial error is made in the ests. of the enthalpy and entropy of adsorption when neglecting the pressure effects associated with the change in the molar

volume of **insulin**. This work proves that the average column pressure must be kept constant during thermodn. measurements of **protein** adsorption consts., especially in RPLC and HIC. The authors' results show also that there is a critical **temperature**, Tc ≈53. **degree.**, at which ln(k') is maximum and the **insulin** adsorption process changes from an exothermic to an endothermic one. This **temperature** dets. also the transition point in the mol. mechanism of **insulin** adsorption that involves successive unfolding of the **protein** chain.

ST **insulin** adsorption reversed phase HPLC column pressure **temp**

IT Adsorption
Adsorption enthalpy
Adsorption entropy
Free energy
Protein folding
Reversed phase HPLC
(column pressure and **temperature** effects on **insulin** adsorption behavior in isocratic reversed-phase HPLC)

IT **Temperature**
(**high**; column pressure and **temperature** effects on **insulin** adsorption behavior in isocratic reversed-phase HPLC)

IT Pressure
(hydrostatic; column pressure and **temperature** effects on **insulin** adsorption behavior in isocratic reversed-phase HPLC)

IT Molar volume
(**insulin**; column pressure and **temperature** effects on **insulin** adsorption behavior in isocratic reversed-phase HPLC)

IT **9004-10-8P**, **Insulin**, preparation
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); PREP (Preparation); PROC (Process)
(column pressure and **temperature** effects on **insulin** adsorption behavior in isocratic reversed-phase HPLC)

RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L84 ANSWER 11 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2002:441430** HCAPLUS
DN **137:153910**
ED Entered STN: 12 Jun 2002
TI Bioprocess development for the cultivation of human T-lymphocytes
AU Hilbert, U.; Bohnenkamp, H.; Noll, T.
CS Institute of Biotechnology 2, Julich, 52425, Germany
SO Animal Cell Technology: From Target to Market, Proceedings of the ESACT Meeting, 17th, Tyloesand, Sweden, June 10-14, 2001 (**2001**), 503-509. Editor(s): Lindner-Olsson, Elisabeth; Chatzissavidou, Nathalie; Luellau, Elke. Publisher: Kluwer Academic Publishers, Dordrecht, Neth. CODEN: 69CRYK; ISBN: 1-4020-0264-5
DT Conference
LA English
CC 16-6 (**Fermentation** and Bioindustrial Chemistry)
AB The authors cultured human mononuclear T-lymphocytes in suspension to determine the effects of various operational parameters on cell growth. The effects of pH, oxygen tension, osmolality, **interleukin** 2 concentration, **temperature** and feeding strategy on cell proliferation were investigated.
ST bioprocess development cultivation human T lymphocytes
IT pH
(biol. effects of; bioprocess development for cultivation of human

T-lymphocytes)
IT Cell proliferation
Human
Osmolality
T cell (lymphocyte)
Temperature effects, biological
(bioprocess development for cultivation of human T-lymphocytes)
IT **Interleukin 2**
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(bioprocess development for cultivation of human T-lymphocytes)
IT Animal tissue culture
(fed-batch; bioprocess development for cultivation of human T-lymphocytes)
IT Bioreactors
(stirred-tank; bioprocess development for cultivation of human T-lymphocytes)
IT Animal tissue culture
(suspension; bioprocess development for cultivation of human T-lymphocytes)
IT 7782-44-7, Oxygen, processes
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(dissolved; bioprocess development for cultivation of human T-lymphocytes)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L84 ANSWER 12 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2002:9635** HCAPLUS
DN **136:198956**
ED Entered STN: 04 Jan 2002
TI **Temperature** downshift increases recombinant cytokine titer in Streptomyces lividans fermentation
AU Yun, Soon-Il; Yahya, Ahmad R. M.; Cossar, Doug; Anderson, William A.; Scharer, Jeno M.; Moo-Young, Murray
CS Department of Chemical Engineering, University of Waterloo, Waterloo, ON, N2L 3G1, Can.
SO Biotechnology Letters (**2001**), 23(23), 1903-1905
CODEN: BILED3; ISSN: 0141-5492
PB Kluwer Academic Publishers
DT Journal
LA English
CC 16-1 (**Fermentation** and Bioindustrial Chemistry)
AB Recombinant human **interleukin**-3 (rhIL-3) production by a Streptomyces lividans strain is subject to severe proteolytic degradation Human **interleukin**-3 (rhIL-3) concentration in the culture supernatant typically reaches 100-120 mg l-1 about 20 h after inoculation, but the titer drops rapidly as the result of proteolysis. Reducing the culture **temperature** at this point has a dramatic effect on product yield, increasing the final concentration in the supernatant at least two-fold.
ST Streptomyces recombinant cytokine ferm **temp**
IT Streptomyces lividans
(recombinant; **temperature** downshift increases recombinant cytokine titer in Streptomyces lividans fermentation)
IT **Fermentation**
Human
Protein degradation
Temperature effects, biological
(**temperature** downshift increases recombinant cytokine titer in Streptomyces lividans fermentation)
IT **Interleukin 3**

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(**temperature** downshift increases recombinant cytokine titer in Streptomyces lividans fermentation)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L84 ANSWER 13 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2001:816959** HCAPLUS
DN **135:356845**
ED Entered STN: 09 Nov 2001
TI Whole cell and cell-debris free polysaccharide
IN Mikolajczak, Marcia; Yamazak, Motohide; Pollock, Thomas J.
PA Shin-Etsu Bio, Inc., USA; Shin-Etsu Chemical Co., Ltd.
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12P019-04
ICS C12N001-20; C07H001-00
CC 16-4 (**Fermentation** and Bioindustrial Chemistry)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001083802	A1	20011108	WO 2001-US13773	20010426 <--
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002031808	A1	20020314	US 2001-838650	20010419 <--
US 6602997	B2	20030805		
CA 2407313	AA	20011108	CA 2001-2407313	20010426 <--
EP 1283896	A1	20030219	EP 2001-930913	20010426 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI US 2000-200082P	P	20000427 <--		
US 2001-838650	A	20010419 <--		
WO 2001-US13773	W	20010426 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001083802	ICM	C12P019-04
	ICS	C12N001-20; C07H001-00
US 2002031808	ECLA	C12P019/04 <--

AB The present invention provides for a method for obtaining a polysaccharide substantially free from whole bacterial cells and bacterial cell debris. The process comprises initially, a fermentation of a Sphingomonas bacterium, which produces the polysaccharide into the fermentation broth. The fermentation broth is then diluted with an equal volume of deionized water and the polysaccharide is partially hydrolyzed by autoclaving the fermentation broth to a **temp**. in excess of 100 °C for a time period from about ten minutes to about one hour. The bacterial cells are then removed from the polysaccharide by centrifugation of the fermentation broth and recovery of a supernatant aqueous liquid The polysaccharide is precipitated from the supernatant aqueous liquid by adding a water miscible solvent to the supernatant which does not

react with the polysaccharide and in which the polysaccharide is insol. The polysaccharide is then harvested by centrifugation, redissolved and precipitated with the solvent.

ST Sphingomonas exopolysaccharide cell free

IT **Heating**
(autoclaving; whole cell and cell-debris free polysaccharide)

IT **Fermentation**
(batch; whole cell and cell-debris free polysaccharide)

IT Polysaccharides, preparation
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(exopolysaccharides; whole cell and cell-debris free polysaccharide)

IT Gene, microbial
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(rhsA; whole cell and cell-debris free polysaccharide)

IT Gene, microbial
Gene, microbial
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(rhsC; whole cell and cell-debris free polysaccharide)

IT Gene, microbial
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(rhsD; whole cell and cell-debris free polysaccharide)

IT Gene, microbial
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(spsB; whole cell and cell-debris free polysaccharide)

IT Dilution
Genetic engineering
Precipitation (chemical)
Sphingomonas
(whole cell and cell-debris free polysaccharide)

IT 7732-18-5, Water, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(deionized; whole cell and cell-debris free polysaccharide)

IT 372101-63-8P 372101-64-9P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(structural repeating unit; whole cell and cell-debris free polysaccharide)

IT 50-99-7, Dextrose, biological studies 154-17-6, 2-Deoxyglucuronic acid 3615-41-6, Rhamnopyranose
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(whole cell and cell-debris free polysaccharide)

IT 9014-01-1, Bioprase 39450-01-6, **Proteinase** K 166433-41-6, Multifect 323198-36-3, Protex 6L
RL: BPR (Biological process); BSU (Biological study, unclassified); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(whole cell and cell-debris free polysaccharide)

IT 64-17-5, Ethanol, processes 67-56-1, Methanol, processes 67-63-0, Isopropanol, processes 67-64-1, Acetone, processes 71-36-3, 1-Butanol, processes 71-41-0, Amyl alcohol, processes 75-65-0, tert-Butanol, processes 78-83-1, Isobutanol, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(whole cell and cell-debris free polysaccharide)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L84 ANSWER 14 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2001:782271** HCAPLUS
DN **136:354240**
ED Entered STN: 29 Oct 2001
TI Fouling of fermentation media in continuous sterilization in the solid **heat** transfer
AU Gondorf, Andreas Harald
CS Dortmund, Germany
SO Fortschritt-Berichte VDI, Reihe 3: Verfahrenstechnik (**2001**), 697, i-ix,1-112
CODEN: FVVEFK; ISSN: 0178-9503
PB VDI Verlag GmbH
DT Journal
LA German
CC 16-9 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 9
AB This study examines the formation of deposits (fouling) of fermentation media during HTST sterilization in compact **heat** exchangers. Fouling on **heat** exchanged surfaces leads to a reduced **heat** transfer, to an increased pressure drop and to clogging small cross sections. Thus a successful sterilization and product quality are endangered limiting the application of compact **heat** exchangers.
The examination of a large number of different fermentation media shows that fouling depends on the type and the concentration of the media ingredients. In particular complex media components as corn steep liquor, yeast extract and molasses lead to a strong deposition. In spite of the large variety of media components the deposits consist only of few substances, mainly of CaHPO4 and MgHPO4 as well as denatured **proteins** (e. g. serum **albumins**). Crystalline deposits form hard and rough fouling layers, while **protein** containing fouling layers form a softer and smoother surface. Both types of fouling reach a thickness over 100 μn. Higher **temps.** promote the fouling process, although the **temperature** dependence of deposition is not very pronounced. The activation energies are 24 kJ/mol for phosphate deposition and 73 kJ/mol for fouling of serum **albumin** above 88 'C. Only in case of serum **albumin** fouling below 88 'C a strong **temperature** dependence and an activation energy of 353 kJ/mol can be observed Thus the activation energy of the deposition process is low compared to the one of spore destruction or virus inactivation. Because of the mass transfer limitation a higher fluid velocity accelerates initially the fouling rate but decreases it later on by eroding deposits. Deposition can be reduced by using additives, changing the media pH and modifying the **heat** exchanger's surface. The effect of additives and a change in pH is based on improving the solubility of the foulants or decreasing its adhesion potential. Thus the fouling rate can be reduced up to 98% and the induction time extended up to ten times, Electropolished surfaces and applying antifouling coatings decrease the number of nucleation sites and/or the adhesion forces between foulants and the **heat** exchangers surface leading to a up to five times longer induction time. All types of deposits are removable by CIP (cleaning in place) techniques. Crystalline fouling layers can be dissolved by acids and chelating agents while **protein** containing deposits are hydrolyzed by caustic agents or proteases. Deposits consisting of salts and **proteins** require a sequential application of acids/chelating agents and bases/proteases. To predict the fouling process and optimize the process conditions **heat** and mass transfer as well as chemical reactions are modelled. Dynamic simulation is carried out using the simulation tool gPROMS. Information about **temperature** profiles, deposits distribution in the capillary and evolution of fouling processes is obtained. Thus the effects of fouling can be considered in the design of sterilization processes.

ST fouling culture media fermn sterilization **heat** exchanger
IT Silanes
RL: TEM (Technical or engineered material use); USES (Uses)
(alkylalkoxy; antifouling treatment/agents against fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT Coating process
Heat treatment
Surface treatment
(antifouling treatment/agents against fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT Plastics, uses
RL: TEM (Technical or engineered material use); USES (Uses)
(antifouling treatment/agents against fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT Microorganism
(biofilm; fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT Industrial liquors
(corn steep liquor; fouling of fermentation media in continuous sterilization
in compact **heat** exchangers influenced by culture medium composition)
IT Polishing
(electrochem.; antifouling treatment/agents against fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT Malt
Yeast
(extract; fouling of fermentation media in continuous sterilization in compact
heat exchangers influenced by culture medium composition)
IT Crystallization
(fouling anal. of fermentation media in continuous sterilization in compact **heat** exchangers)
IT Antifouling agents
Culture media
Fermentation
Fouling
Heat exchangers
Heat transfer
Simulation and Modeling, physicochemical
Sterilization and Disinfection
(fouling of fermentation media in **continuous** sterilization in compact **heat** exchangers)
IT **Proteins**
Salts, biological studies
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT Buffers
Meat extracts
Milk
(fouling of fermentation media in continuous sterilization in compact **heat** exchangers influenced by culture medium composition)
IT Molasse
Peptones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fouling of fermentation media in continuous sterilization in compact **heat** exchangers influenced by culture medium composition)
IT **Albumins, biological studies**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serum; fouling of fermentation media in continuous sterilization in compact **heat** exchangers influenced by culture medium composition)

IT Polyphosphoric acids
RL: TEM (Technical or engineered material use); USES (Uses)
(sodium salts; antifouling treatment/agents against fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT **Lactalbumins**
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(α-; fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT Lactoglobulins
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(β-; fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT 9001-92-7, Protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antifouling treatment/agents against fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT 60-00-4, EDTA, uses 64-19-7, Acetic acid, uses 77-92-9, Citric acid, uses 7697-37-2, Nitric acid, uses 7722-88-5, Sodium pyrophosphate
RL: TEM (Technical or engineered material use); USES (Uses)
(antifouling treatment/agents against fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT 1310-73-2, Sodium hydroxide, uses
RL: TEM (Technical or engineered material use); USES (Uses)
(combined with HCl; antifouling treatment/agents against fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT 7647-01-0, Hydrochloric acid, uses
RL: TEM (Technical or engineered material use); USES (Uses)
(combined with NaOH; antifouling treatment/agents against fouling of fermentation media in continuous sterilization in compact **heat** exchangers)
IT 7757-86-0, Magnesium hydrogen phosphate 7757-93-9, Calcium hydrogen phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fouling anal. of fermentation media in continuous sterilization in compact **heat** exchangers)
IT 50-99-7, Glucose, biological studies 57-13-6, Urea, biological studies 57-50-1, Saccharose, biological studies 7439-95-4, Magnesium, biological studies 7440-70-2, Calcium, biological studies 7783-20-2, Ammonium sulfate, biological studies 14265-44-2, Phosphate, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fouling of fermentation media in continuous sterilization in compact **heat** exchangers influenced by culture medium composition)
RE.CNT 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L84 ANSWER 15 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:749500 HCAPLUS
DN 135:256329
ED Entered STN: 15 Oct 2001

TI Changes of immunoreactive properties of cow milk **proteins** as a result of technological processing
AU Wroblewska, Barbara; Jedrychowski, Lucjan
CS Inst. Rozrodu Zwierzat i Badan Zywnosci, Polska Akad. Nauk, Olsztyn, 10-747, Pol.
SO Biotechnologia (**2001**), (3), 189-201
CODEN: BIECEV; ISSN: 0860-7796
PB Instytut Chemii Bioorganicznej PAN
DT Journal
LA Polish
CC 17-4 (Food and Feed Chemistry)
AB Pasteurization of milk can decrease whey **protein** immunoreactivity (allergenicity). The effects of milk pasteurization (**60**, 72, 80 and 90°C and various duration), ultrasonic and microwave treatment, and fermentation on milk whey **protein** (α- **lactalbumin** and β-lactoglobulin) immunoreactivity were examined The immunoreactivity was determined by indirect and competitive ELISA. The severe pasteurization conditions (90. **degree**.C, 15 min) decreased the immunoreactivity of α- **lactalbumin** and β-lactoglobulin to 12.72 and 18.74%, resp. Ultrasonic and microwave processes were much more effective than severe pasteurization. Ultrasonic treatment at 50°C for 1 h decreased the α- **lactalbumin** and β-lactoglobulin immunoreactivity to 0.88 and 6.42%, resp. Microwaving at 98. **degree**.C for 2 min. decreased the α- **lactalbumin** and β-lactoglobulin immunoreactivity to 1.37 and 12.86%, resp. Lactic acid fermentation decreased the milk **protein** immunoreactivity to <1%. The fermented products retained good organoleptic properties (acid taste and aroma). The allergenicity of fermented milk prepns. examined by skin tests in patients with food allergies showed that the allergenicity of both whey **proteins** was only slightly attenuated.
ST milk pasteurization microwave ultrasound fermn **lactalbumin** lactoglobulin immunoreactivity decrease
IT **Fermentation**
Microwave heating
Pasteurization
Sound and Ultrasound
(cow milk α- **lactalbumin** and β-lactoglobulin **proteins** immunoreactivity decrease by pasteurization, microwave, ultrasound and fermentation processing)
IT Allergens
RL: BPR (Biological process); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); PROC (Process); USES (Uses)
(cow milk α- **lactalbumin** and β-lactoglobulin **proteins** immunoreactivity decrease by pasteurization, microwave, ultrasound and fermentation processing)
IT **Proteins**, specific or class
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(whey; cow milk α- **lactalbumin** and β-lactoglobulin **proteins** immunoreactivity decrease by pasteurization, microwave, ultrasound and fermentation processing)
IT **Lactalbumins**
RL: BPR (Biological process); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); PROC (Process); USES (Uses)
(α-; cow milk α- **lactalbumin** and β-lactoglobulin **proteins** immunoreactivity decrease by pasteurization, microwave, ultrasound and fermentation processing)
IT Lactoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); PROC (Process); USES (Uses)
(β-; cow milk α- **lactalbumin** and β-lactoglobulin **proteins** immunoreactivity decrease by

pasteurization, microwave, ultrasound and fermentation processing)

L84 ANSWER 16 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2001:538910** HCAPLUS
DN **137:124215**
ED Entered STN: 26 Jul 2001
TI Purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production
AU Fan, C.-H.; Lee, C.-K.
CS Department of Chemical Engineering, National Taiwan University of Science and Technology, Taipei, 10617, Taiwan
SO Biochemical Engineering Journal (**2001**), 8(2), 157-164
CODEN: BEJOFV; ISSN: 1369-703X
PB Elsevier Science S.A.
DT Journal
LA English
CC 16-1 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 7, 11
AB Hydantoinase could be extracted from adzuki bean by a simple separation process.
The mol. weight of the partially purified hydantoinase determined by MALDI-TOF mass spectrometry was 52.5 kDa. The enzyme was determined to be D-specific and preferred the substrate D-phenylhydantoin (PH) rather than D-p-hydroxy-phenylhydantoin (pHPH). Its specific activity towards PH was about sixfold of that towards pHPH. The enzyme retained 76% of its activity after incubation at 40°C for 6 days. Its immobilization was easily achieved by mixing the enzyme solution with fine polyglutaraldehyde (PGL) particles (<10 μm). In order to enlarge the size of the immobilized enzymes for easy recovery, the fine immobilized enzyme particles were then entrapped in the calcium alginate bead and hardened with polyethyleneimine (PEI). The immobilized D-hydantoinase could transform 1% (w/v) PH into N-carbamoyl-D-phenylglycine (d-CPG) with >95% conversion and very good stability that no appreciable activity loss was observed after five repeated batch reactions at 40°C.
ST adzaki bean hydantoinase immobilization
IT Enzyme kinetics
(Michaelis-Menten; purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production)
IT Structure-activity relationship
(enzyme substrate; purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production)
IT Immobilization, molecular or cellular
(enzyme; purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production)
IT **Temperature**
pH
(optimum for enzyme activity; purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production)
IT Encapsulation
Precipitation (chemical)
Ultrafiltration
Vigna angularis
(purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production)
IT 9030-74-4P, D-Hydantoinase
RL: BCP (Biochemical process); CAT (Catalyst use); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production)
IT 89-24-7, Phenylhydantoin 41807-35-6
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)

(purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production)
IT 6489-76-5P, N-Carbamoyl-D-phenylglycine
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production)
IT 9005-35-0, Calcium alginate 29257-65-6, Polyglutaraldehyde
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production)
IT 9002-98-6 26913-06-4, Poly[imino(1,2-ethanediyl)]
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(purification of D-hydantoinase from adzuki bean and its immobilization for N-carbamoyl-D-phenylglycine production)
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Dinelli, D; Enzyme Engineering 1978, V3, P477
(2) Lee, C; Enzyme Microb Technol 1996, V19, P623 HCAPLUS
(3) Lee, C; Enzyme Microb Technol 1999, V24, P659 HCAPLUS
(4) Lee, S; Appl Microbiol Biotechnol 1955, V43, P270
(5) Margel, S; Ind Eng Chem Prod Res Dev 1982, V21, P343 HCAPLUS
(6) Margel, S; Macromolecules 1980, V13, P19 HCAPLUS
(7) Mazus, B; Phytochemistry 1972, V11, P77 HCAPLUS
(8) Moller, A; Enzyme Microb Technol 1988, V10, P618
(9) Morin, A; Appl Microbiol Biotechnol 1986, V25, P91 HCAPLUS
(10) Morin, A; Enzyme Microb Technol 1993, V15, P208 HCAPLUS
(11) Olivieri, R; Enzyme Microb Technol 1979, V1, P201 HCAPLUS
(12) Runser, S; FEBS 1993, V213, P1315 HCAPLUS
(13) Syldatk, C; Appl Microbiol Biotechnol 1999, V51, P293 HCAPLUS
(14) Takahashi, S; J Ferment Technol 1979, V4, P328
(15) Tintemann, H; Comp Biochem Physiol B 1987, V88, P943
(16) Wallach, D; J Biol Chem 1957, V226, P277 HCAPLUS

L84 ANSWER 17 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2001:72524** HCAPLUS
DN **134:99688**
ED Entered STN: 01 Feb 2001
TI Preparation of **protein oligopeptide**
IN Wang, Youyong
PA Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
IC ICM C12P021-00
CC 16-5 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 17
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1258750	A	20000705	CN 1999-120131	19991217 <--
	CN 1117873	B	20030813		
PRAI	CN 1999-120131		19991217 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
CN 1258750	ICM	C12P021-00

AB The process comprises high-speed agitation of egg **albumin**, adding water, **heating** at 70-80° for 10-20 min, hydrolyzing with pepsin in acidic solution at 45° for 2-3 h,

adding stabilizer Ca2+, regulating pH to 7.0-7.5, hydrolyzing with trypsin at 45- 50° for 8-10 h, deactivating of the enzyme by boiling for 15 min, filtering, and concentrating The method eliminated pollution and gives products having good bioavailability. The **oligopeptides** are useful for manufacturing food, cosmetic, and pharmaceutical.

ST **oligopeptide** enzymic prepn egg **albumin**

IT **Peptides**, biological studies
RL: BPN (Biosynthetic preparation); FFD (Food or feed use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**oligopeptides**; preparation of **protein oligopeptide**)

IT Cosmetics
Food
Stabilizing agents
Temperature
pH
(preparation of **protein oligopeptide**)

IT **Protein** hydrolyzates
RL: BPN (Biosynthetic preparation); FFD (Food or feed use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **protein oligopeptide**)

IT **Albumins, biological studies**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of **protein oligopeptide**)

IT 14127-61-8, Calcium (+2), biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(preparation of **protein oligopeptide**)

IT 9001-75-6, Pepsin 9002-07-7, Trypsin
RL: CAT (Catalyst use); USES (Uses)
(preparation of **protein oligopeptide**)

L84 ANSWER 18 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2000:900629** HCAPLUS
DN **134:42025**
ED Entered STN: 22 Dec 2000
TI Recovery of isoquercetin from fermentation-derived bioflavonoid pastes by extraction using water and methyl acetate
IN Buchholz, Herwig; Jungnitz, Michael; Grund, Michael; Rosskopf, Ralf; Hartner, Hartmut
PA Merck Patent G.m.b.H., Germany
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM C07D311-60
ICS C07D311-30
CC 26-4 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): **16**, 33, 48

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000076992	A1	20001221	WO 2000-EP5182	20000606 <--

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19927425	A1	20001221	DE 1999-19927425	19990616	<--
CA 2374747	AA	20001221	CA 2000-2374747	20000606	<--
EP 1187823	A1	20020320	EP 2000-940322	20000606	<--
EP 1187823	B1	20030820			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

BR 2000011628	A	20020514	BR 2000-11628	20000606	<--
JP 2003502323	T2	20030121	JP 2001-503850	20000606	<--
AT 247651	E	20030915	AT 2000-940322	20000606	<--
ES 2204625	T3	20040501	ES 2000-940322	20000606	<--
US 6683164	B1	20040127	US 2002-9485	20020510	<--
PRAI DE 1999-19927425	A	19990616	<--		
WO 2000-EP5182	W	20000606	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 2000076992	ICM	C07D311-60	
	ICS	C07D311-30	
DE 19927425	ECLA	C07D311/28	<--
US 6683164	ECLA	C07D311/28	<--

AB High-purity isoquercetin is obtained from bioflavonoid fermentation pastes (i.e., from mother-liquor residues which are produced during the recovery of flavonoids) by extraction with a solvent mixture of Me acetate and water at 35-50° for ≥30 min, thinning the exts. with water, distilling the Me acetate from the extract under atmospheric pressure, quickly **cooling** the aqueous distillation bottoms to 10° at which point isoquercetin begins to precipitate, and then filtering and drying the isoquercetin.

ST isoquercetin extn bioflavonoid fermn paste

IT Flavonoids
RL: PEP (Physical, engineering or chemical process); REM (Removal or disposal); PROC (Process)
(bioflavonoids; recovery of isoquercetin from fermentation-derived bioflavanoid pastes by extraction using water and Me acetate)

IT **Precipitation (chemical)**
(of extracted isoquercetin)

IT Distillation
(recovery of isoquercetin from fermentation-derived bioflavonoid pastes by extraction using water and Me acetate and)

IT **Cooling**
(recovery of isoquercetin from fermentation-derived bioflavonoid pastes by extraction using water and Me acetate and distillation and)

IT Extraction
(solid-phase; recovery of isoquercetin from fermentation-derived bioflavanoid pastes by extraction using water and Me acetate)

IT 1066-33-7, Ammonium bicarbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(buffer; in the recovery of isoquercetin from fermentation-derived bioflavonoid pastes by extraction using water and Me acetate)

IT 117-39-5, Quercetin
RL: REM (Removal or disposal); PROC (Process)
(in the recovery of isoquercetin from fermentation-derived bioflavonoid pastes by extraction using water and Me acetate)

IT 482-35-9P, Isoquercetin
RL: PUR (Purification or recovery); PREP (Preparation)
(recovery of isoquercetin from fermentation-derived bioflavonoid pastes by extraction using water and Me acetate)

IT 153-18-4, Rutin
RL: REM (Removal or disposal); PROC (Process)
(recovery of isoquercetin from fermentation-derived bioflavonoid pastes by extraction using water and Me acetate)

IT 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(solvent; recovery of isoquercetin from fermentation-derived bioflavonoid pastes by extraction using water and Me acetate)
IT 79-20-9, Methyl acetate
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(solvent; recovery of isoquercetin from fermentation-derived bioflavonoid pastes by extraction using water and Me acetate)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; 1967, 17, P7729 HCAPLUS
(2) Krolikowska, M; ROCZ CHEM 1967, V41(3), P529 HCAPLUS
(3) Merck Patent Gmbh; WO 0026399 A 2000

L84 ANSWER 19 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:693193 HCAPLUS
DN 134:4072
ED Entered STN: 03 Oct 2000
TI Influence of induction conditions on the expression on human **interleukin**-6 in recombinant Escherichia coli
AU Zhang, Ying; Gu, Li-Na; Gan, Yi-Ru; Liu, Jin-Shen; Wang, He-Ling
CS School of Chemical Engineering &. Technology, Tianjin University, Tianjin, 300072, Peop. Rep. China
SO Huaxue Fanying Gongcheng Yu Gongyi (**2000**), 16(3), 275-280
CODEN: HFGGEU; ISSN: 1001-7631
PB Zhejiangsheng Chuban Duiwai Maoyi Gongsi
DT Journal
LA Chinese
CC 16-2 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 3
AB The fermentation conditions under which the human **interleukin**-6 (hIL-6) in recombinant E. Coli containing the **temperature** sensitive plasmid pKpL3a at high level on the shaker flask were investigated. The objective was to find the influence of induction strategies on the growth of recombinant cells and the expression of hIL-6. Several means of the **thermal** induction were used in order to enhance expression of hIL-6. The results indicated that in such a strategy of that the fermentation is carried out in 2 XYT medium, 30°, allowing the OD600 of recombinant E. Coli up to 1.5, then the **temperature** is increased to 42° or **40°** retaining at least 1h, followed by the **temperature** is lowered back to 37.**degree**. for 3h, the final expression of hIL-6, which is only 20% by single **temperature** upshift to 42° or **40.** **degree.**, could be enhanced to 32%. The induction time period is less than 1h, it will not give sufficiently high expression of hIL-6.
ST Escherichia recombinant human **interleukin** 6 manuf; IL6 expression Escherichia induction **temp**
IT Gene
(expression; influence of induction conditions on expression on human **interleukin**-6 in recombinant e. coli)
IT Culture media
Escherichia coli
Fermentation
Temperature
(influence of induction conditions on expression on human **interleukin**-6 in recombinant e. coli)
IT **Interleukin 6**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(of human; influence of induction conditions on expression on human **interleukin**-6 in recombinant e. coli)

IT Plasmids
(pKpL3a; influence of induction conditions on expression on human **interleukin**-6 in recombinant e. coli)

L84 ANSWER 20 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2000:96123** HCAPLUS
DN **132:119578**
ED Entered STN: 10 Feb 2000
TI Method for the enzymic elimination of **albumin** after the cell culturing procedure
IN Weber, Ekkehard; Guenther, Dagmar
PA Martin-Luther-Universitaet Halle-Wittenberg, Germany
SO Ger., 4 pp.
CODEN: GWXXAW
DT Patent
LA German
IC ICM C07K001-14
CC 9-11 (Biochemical Methods)
Section cross-reference(s): 7, **16**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19852216	C1	20000210	DE 1998-19852216	19981112 <--
PRAI DE 1998-19852216		19981112 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 19852216	ICM	C07K001-14
DE 19852216	ECLA	C07K001/14 <--

AB The invention concerns a method for the elimination of the cell culture medium component **albumin** upon the completion of the culturing in order to facilitate the purification of **protein** products by activating endogenic or exogenic procathepsin D/cathepsin D at acidic pH (pH 2.5-4.0) and low **temperature** (4-10 °C) in conjunction with dialysis for the removal of the degraded **albumin**; followed by dialysis against a pH 7.0-8.2 buffer to block the enzymic activity. Procathepsin D and cathepsin D are active at acidic pH; the low **temperature** prevents the degradation of the target **proteins.**
ST cell culture medium **albumin** removal procathepsin cathepsin D dialysis
IT **Temperature**
(**low**; method for enzymic elimination of **albumin** after cell culturing procedure)
IT Animal tissue culture
Biotechnology
Buffers
Culture media
Dialysis
pH
(method for enzymic elimination of **albumin** after cell culturing procedure)
IT **Proteins**, general, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(method for enzymic elimination of **albumin** after cell culturing procedure)
IT **Albumins, reactions**
RL: RCT (Reactant); REM (Removal or disposal); PROC (Process); RACT (Reactant or reagent)
(method for enzymic elimination of **albumin** after cell culturing procedure)
IT **Proteins**, general, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(separation; method for enzymic elimination of **albumin** after cell culturing procedure)
IT 9025-26-7, Cathepsin D 86921-29-1, Cathepsin D, pro-
RL: CAT (Catalyst use); USES (Uses)
(method for enzymic elimination of **albumin** after cell culturing procedure)

L84 ANSWER 21 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1999:595213** HCAPLUS
DN **131:213188**
ED Entered STN: 21 Sep 1999
TI A process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants
IN Garger, Stephen J.; Holtz, R. Barry; Mcculloch, Michael J.; Turpen, Thomas H.
PA Biosource Technologies, Inc., USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-415
ICS C12N007-02
CC 16-1 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 11
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9946288	A2	19990916	WO 1999-US5056	19990309 <--
	WO 9946288	A3	20000120		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6037456	A	20000314	US 1998-37751	19980310 <--
	US 6033895	A	20000307	US 1999-259741	19990225 <--
	CA 2322616	AA	19990916	CA 1999-2322616	19990309 <--
	AU 9930725	A1	19990927	AU 1999-30725	19990309 <--
	AU 747647	B2	20020516		
	EP 1062235	A2	20001227	EP 1999-912327	19990309 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002506080	T2	20020226	JP 2000-535664	19990309 <--
	US 6303779	B1	20011016	US 1999-466422	19991217 <--
	US 2003049813	A1	20030313	US 2001-962527	20010924 <--
	US 6740740	B2	20040525		
	US 2004166026	A1	20040826	US 2004-781448	20040218 <--
	US 2004171813	A1	20040902	US 2004-828029	20040420 <--
PRAI	US 1998-37751	A	19980310 <--		
	US 1999-259741	A1	19990225 <--		
	WO 1999-US5056	W	19990309 <--		
	US 1999-466422	A1	19991217 <--		
	US 2001-962527	A1	20010924 <--		
	US 2001-970150	A3	20011003 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

WO 9946288	ICM	C07K014-415
	ICS	C12N007-02
WO 9946288	ECLA	C07K014/415; C07K016/00; C12N007/00; C12N015/82A4A; C12N015/82C4D2; C12N015/82C4D; C12N015/82C4 <--
US 6037456	ECLA	C07K014/415; C07K016/00; C12N007/00; C12N015/82A4A; C12N015/82C4; C12N015/82C4D; C12N015/82C4D2 <--
US 6033895	ECLA	C07K016/00; C12N007/00; C12N007/02 <--
US 6303779	ECLA	C07K014/415; C07K016/00; C12N007/00; C12N007/02; C12N015/82A4A; C12N015/82C4; C12N015/82C4D; C12N015/8C4D2 <--
US 2003049813	ECLA	C07K014/415; C12N015/82C4; C12N015/82C4D; C12N015/82C4D2; C07K016/00; C12N007/00; C12N007/02; C12N015/2A4A <--
US 2004166026	ECLA	C07K014/415; C07K016/00; C12N007/00; C12N007/02; C12N015/82A4A; C12N015/82C4; C12N015/82C4D; C12N015/8C4D2 <--
US 2004171813	ECLA	C07K014/415; C07K016/00; C12N007/00; C12N007/02; C12N015/82A4A; C12N015/82C4; C12N015/82C4D; C12N015/8C4D2 <--

AB The present invention features a method for isolating and purifying viruses, **proteins** and **peptides** of interest from a plant host which is applicable on a large scale. Moreover, the present invention provides a more efficient method for isolating viruses, **proteins** and **peptides** of interest than those methods described in the prior art. In general, the present method of isolating viruses, **proteins** and **peptides** of interest comprises the steps of homogenizing a plant to produce a green juice, adjusting the pH of and **heating** the green juice, separating the target species, either virus or **protein/peptide**, from other components of the green juice by one or more cycles of centrifugation, resuspension, and ultrafiltration, and finally purifying virus particles by such procedure as PEG-precipitation or purifying **proteins** and **peptides** by such procedures as chromatog. and/or salt precipitation The invention also concerns transgenic plants and the isolation of viral **proteins** and/or other fusion **proteins.**

ST transgenic plant virus **protein peptide** purifn ultrafiltration chromatog

IT Immunoglobulins
RL: BMF (Bioindustrial manufacture); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(A, secretory; a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT Plant virus
(Rice necrosis; a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT Alfalfa mosaic virus
Biotechnology
Bromovirus
Capillovirus
Carlavirus
Carmovirus
Caulimovirus
Centrifugation
Chromatography
Closterovirus
Commelina yellow mottle virus
Comovirus
Dianthovirus
Fabavirus
Furovirus

Geminiviridae
Homogenization
Leaf
Luteovirus
Marafivirus
Necrovirus
Nepovirus
Pea enation mosaic virus
Plant (Embryophyta)
Plant tissue culture
Potexvirus
Potyvirus
Precipitation (chemical)
Purification
Reoviridae
Sobemovirus
Temperature
Tenuivirus
Tobacco (Nicotiana benthamiana)
Tobacco mosaic virus
Tobamovirus
Tobravirus
Tombusvirus
Tymovirus
Ultracentrifugation
Vaccines
Virus
pH
(a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT Antibodies
Antigens
Enzymes, preparation
Fusion **proteins** (chimeric **proteins**)
Hormones, animal, preparation
Interleukin 1
Interleukin 10
Interleukin 11
Interleukin 12
Interleukin 2
Interleukin 3
Interleukin 4
Interleukin 5
Interleukin 6
Interleukin 7
Interleukin 8
Interleukin 9
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT Alkaloids, biological studies
Carbohydrates, biological studies
Polysaccharides, biological studies
Trichosanthin
Vitamins
RL: BMF (Bioindustrial manufacture); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT **Peptides**, biological studies
Proteins, specific or class

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT Polyoxyalkylenes, uses
RL: NUU (Other use, unclassified); USES (Uses)
(a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT Flavor
(compds.; a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT Plant virus
(cryptovirus; a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT **Proteins**, general, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(separation; a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT Plant (Embryophyta)
(transgenic; a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT 9001-28-9P, Blood-coagulation factor IX **9004-10-8P**, **Insulin**, preparation 9007-12-9P, Calcitonin 11096-26-7P, Erythropoietin 12629-01-5P, Human growth hormone 37231-28-0DP, Melittin, derivs. 80802-79-5DP, Cecropin, derivs. 81627-83-0P, Macrophage colony-stimulating factor 83869-56-1P, Granulocyte-macrophage colony-stimulating factor 103220-14-0DP, Defensin, derivs. 113041-69-3DP, Magainin, derivs. 113189-02-9P, Blood-coagulation factor VIII, procoagulant 116229-36-8DP, Bactenecin, derivs. 120668-29-3DP, Cryptdin, derivs. 139639-23-9P, Tissue-type plasminogen activator 140896-21-5DP, Indolicidin, derivs. 143011-72-7P, Granulocyte-colony-stimulating factor 156476-39-0DP, β-Defensin, derivs. 163663-18-1P, Protegrin
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT 9027-23-0P, Ribulose 1,5-diphosphate carboxylase
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT 7681-57-4, Sodium metabisulfite 25322-68-3, PEG
RL: NUU (Other use, unclassified); USES (Uses)
(a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

IT 242799-66-2, RNA (tobacco mosaic virus strain TMV204) 242799-67-3, RNA (tobacco mosaic virus strain TMV261) 242799-68-4, RNA (tobacco mosaic virus strain TMV291) 242799-69-5, RNA (tobacco mosaic virus strain TMV811) 242799-70-8, RNA (tobacco mosaic virus strain TMV861)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; a process for isolating and purifying viruses, soluble **proteins** and **peptides** from plant sources including transgenic plants)

L84 ANSWER 22 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN

AN **1999:45612** HCAPLUS
DN **130:266395**
ED Entered STN: 22 Jan 1999
TI **Temperature**-induced production of recombinant human **insulin** in high-cell density cultures of recombinant Escherichia coli
AU Schmidt, Michael; Babu, Kunnel Raman; Khanna, Navin; Marten, Sabine; Rinas, Ursula
CS Biochemical Engineering Division, GBF National Research Center for Biotechnology, Braunschweig, 38124, Germany
SO Journal of Biotechnology (**1999**), 68(1), 71-83
CODEN: JBITD4; ISSN: 0168-1656
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
CC 16-2 (**Fermentation** and Bioindustrial Chemistry)
AB The construction of expression vectors encoding either the human **insulin** A- or B-chains fused to a synthetic **peptide** and the **temperature**-induced expression of the recombinant genes in Escherichia coli are reported. Using this two-chain approach we also describe the sep. isolation of the **insulin** A- and B-chains from inclusion bodies and their subsequent assembly into native human **insulin.** The production of the **insulin** fusion **proteins** were carried out in high-cell d. fed-batch cultures using a synthetic medium with glucose as sole carbon and energy source. The expression of the recombinant genes by **temperature**-shift in high-cell d. cultures of recombinant E. coli resulted in product yields of grams per L of culture broth, e.g. 4.5 g of **insulin** B-chain fusion **protein** per L of culture broth. This translates into an expression yield of about 800 mg of the **insulin** B-chain per L of culture. Under similar cultivation conditions the expression yield of the **insulin** A-chain corresponds to approx. 600 mg per L of culture. The metabolic burden imposed on the recombinant cells during **temp** .-induced production of **insulin** fusion **proteins** in high-cell d. cultures is reflected in an increased respiratory activity and a reduction of the biomass yield coefficient with respect to glucose.
ST human **insulin** fermn recombinant Escherichia
IT **Fermentation**
(fed-batch; **temperature**-induced production of recombinant human **insulin** in high-cell d. cultures of recombinant Escherichia coli)
IT Escherichia coli
Molecular cloning
Temperature effects, biological
(**temperature**-induced production of recombinant human **insulin** in high-cell d. cultures of recombinant Escherichia coli)
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**temperature**-induced production of recombinant human **insulin** in high-cell d. cultures of recombinant Escherichia coli)
IT **11061-68-0P**, Human **insulin**
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(**temperature**-induced production of recombinant human **insulin** in high-cell d. cultures of recombinant Escherichia coli)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L84 ANSWER 23 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:663916 HCAPLUS
DN 129:315023
ED Entered STN: 21 Oct 1998
TI Chromatographic removal and **heat** inactivation of hepatitis B virus during the manufacture of human **albumin**
AU Adcock, Wayne L.; MacGregor, Andrew; Davies, Jeff R.; Hattarki, Meghan; Anderson, David A.; Goss, Neil H.
CS Bioplasma Division, Research and Development, CSL Limited, Broadmeadows, 3047, Australia
SO Biotechnology and Applied Biochemistry (**1998**), 28(2), 169-178
CODEN: BABIEC; ISSN: 0885-4513
PB Portland Press Ltd.
DT Journal
LA English
CC 16-4 (**Fermentation** and Bioindustrial Chemistry)
AB The purpose of the present study was to examine the efficacy of the chromatog. and pasteurization steps, employed in the manufacture of human **albumin**, in the removal and/or inactivation of hepatitis B virus (HBV). Most human **albumins** manufactured today are prepared from donor plasma by fractionation methods that use precipitation with **cold** ethanol. CSL Limited, an Australian biopharmaceutical company, has recently converted its method of manufacture for **albumin** from a traditional Cohn fractionation method to a method employing chromatog. techniques. A step-by-step validation of virus removal and inactivation was performed on this manufacturing process, which includes a DEAE-Sepharose and CM-Sepharose Fast Flow ion-exchange step, a Sephacryl S200 High-Resolution gel-filtration step and a bulk pasteurization step where product is held at **60** °C for 10 h. HBV partitioning expts. were conducted on scaled-down chromatog. columns with hepatitis B surface antigen (HBsAg) as a marker, whereas the HBV model virus, duck HBV, was used to study the inactivation kinetics during pasteurization. Redns. for HBsAg through the three chromatog. steps resulted in a total log10 decrease of 1.5 log10, whereas more than 6.5 log10 decrease in duck HBV in Albumex 5 was achieved during pasteurization.
ST hepatitis virus **heat** inactivation **albumin** human
IT Chromatography
Hepatitis B virus
Pasteurization
(chromatog. removal and **heat** inactivation of hepatitis B virus during manufacture of human **albumin**)
IT **Temperature effects, biological**

(**heat**; chromatog. removal and **heat** inactivation of hepatitis B virus during manufacture of human **albumin**)

IT **Albumins, preparation**
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(serum; chromatog. removal and **heat** inactivation of hepatitis B virus during manufacture of human **albumin**)

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L84 ANSWER 24 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1997:736747** HCAPLUS
DN **128:21534**
ED Entered STN: 24 Nov 1997
TI New method of preparation of bovine colostral immunoglobulins for parenteral application in calves
AU Semotan, K.; Kalab, D.
CS Czech Rep.
SO Veterinarni Medicina (Prague) (**1997**), 42(9), 249-252
CODEN: VTMDAR; ISSN: 0375-8427

PB Ustav Zemedelskych a Potravinarskych Informaci
DT Journal
LA Czech
CC 15-1 (Immunochemistry)
Section cross-reference(s): **16**

AB A new simple method of preparation of bovine colostral Igs was described using a single step precipitation of skimmed bovine colostrum with dimethyllaurylbenzylammonium bromide (DMLBAB). This quaternary ammonium compound precipitated simultaneously nearly all colostral **proteins** lacking antibody activity. Bovine colostrum was collected mostly during of the first 24 h after calving, at the latest however until 48 h. Isolation of bovine colostral Igs proceeded as follows; one volume of skimmed colostrum containing 3-6% of Igs was slowly precipitated with the same volume of 2% water solution of DMLBAB at pH 7.9-8.1 along with continuous stirring. Turbid mixture was then **heated** to 43-45° and subsequently **cooled** to a room **temperature** standing overnight. Heavy precipitate sedimented down and supernatant fluid containing purified Igs was decanted and clarified by filtration. Residual DMLBAB occurring in the filtrate was removed by passage through a strongly acidic cation exchange column prepared in the Na+ form. Purified colostral Igs were thickened to the required **protein** concentration by ultrafiltration. Dense retentate was clear and became an amber color. Average yield of purified colostral Igs reached 18.8 g/L of skimmed bovine colostrum. Electrophoretic purity of Igs fraction amounted to 90-95%. For parenteral application in calves the above solution of Igs was subsequently adjusted to 9-11% content of **protein**, 0.9% of sodium chloride, pH 7.2, stabilized with 2% of aminoacetic acid and conserved with 0.015% of thiomersal. Finally, the preparation was sterilized by filtration, kept its content of Igs minimally 2 yr at the **temp** . of storage between 2-8° and remained biol. harmless. Using the method described it was not necessary to remove casein from skimmed bovine colostrum prior to the purification of Igs. Hence the method provided a significant short cut especially in laboratory as well as pilot scale production of bovine colostral Igs bringing about a marked economic benefit.

ST cattle colostrum Ig prepn

IT **Temperature effects, biological**
(**heat**; preparation of bovine colostral Igs for parenteral application in calves)

IT Cation exchange chromatography
Cattle
Colostrum
Precipitation (chemical)
Ultrafiltration
(preparation of bovine colostral Igs for parenteral application in calves)

IT Antibodies
Immunoglobulins
RL: AGR (Agricultural use); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bovine colostral Igs for parenteral application in calves)

IT 7281-04-1, Dimethyllaurylbenzylammonium bromide
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(preparation of bovine colostral Igs for parenteral application in calves)

IT 54-64-8, Thiomersal 56-40-6, Aminoacetic acid, uses
RL: MOA (Modifier or additive use); USES (Uses)
(preparation of bovine colostral Igs for parenteral application in calves)

L84 ANSWER 25 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:253319 HCAPLUS
DN 118:253319
ED Entered STN: 26 Jun 1993

TI Effect of induction **temperature** on the PL promoter controlled production of recombinant human **interleukin**-2 in Escherichia coli
AU Lee, In Young; Kim, Myung Kuk; Lee, Sun Bok
CS Genet. Eng. Res. Inst., KIST, Taejon, 305-606, S. Korea
SO Journal of Microbiology and Biotechnology (**1992**), 2(1), 26-34
CODEN: JOMBES; ISSN: 1017-7825
DT Journal
LA English
CC 16-2 (**Fermentation** and Bioindustrial Chemistry)
AB The effect of induction **temperature** of fermentation parameters was investigated extensively using E. coli M5248[pNKM21], a producer of recombinant human **interleukin**-2 (rhIL-2). In this recombinant microorganism, the gene expression of rhIL-2 is regulated by the cI857 repressor and PL promoter system. The recombinant fermentation parameters studied include cell growth, **protein** synthesis, cell viability, plasmid stability, β-lactamase activity, and rhIL-2 productivity. Interrelations of such fermentation parameters were analyzed through a quant. assessment of the exptl. data set obtained at 8 different culture conditions. While the expression of rhIL-2 gene was repressed at culture **temps.** <34° with little effect on other fermentation parameters, under the conditions of rhIL-2 production (36-44**.degree**.), cell growth, plasmid stability, and β-lactamase activity decreased more as induction **temperature** was increased. Although the rhIL-2 content in the insol. **protein** fraction was maximum at **40°**, total rhIL-2 production in the culture volume was highest at the induction **temperature** of 36°. This was in contrast to the previously known optimum induction **temperature** of the PL promoter system (**40**-42°). Explanations for such a discrepancy are proposed based on product formation kinetics, and their implications are discussed in detail.
ST Escherichia prodn **interleukin** PL promoter **temp**
IT Escherichia coli
(**interleukin** 2 production by, **temperature** effect on promoter PL-controlled)
IT **Temperature effects, biological**
(promoter PL-controlled **interleukin** 2 production by Escherichia coli response to)
IT **Lymphokines and Cytokines**
RL: BIOL (Biological study)
(**interleukin 2**, manufacture of human, with Escherichia coli, induction **temperature** effect on PL promoter-controlled)
IT Genetic element
RL: BIOL (Biological study)
(promoter, PL, **interleukin** 2 production by Escherichia coli control by, **temperature** effect on)

L84 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1991:466082 HCAPLUS
DN 115:66082
ED Entered STN: 23 Aug 1991
TI Overexpression of a thermostable lipase gene from Pseudomonas fluorescens in Escherichia coli
AU Chung, Guk Hoon; Lee, Young Phil; Yoo, Ook Joon; Rhee, Joon Shick
CS Dep. Biol. Sci. Eng., Korea Adv. Inst. Sci. Technol., Seoul, 130-650, S. Korea
SO Applied Microbiology and Biotechnology (**1991**), 35(2), 237-41
CODEN: AMBIDG; ISSN: 0175-7598
DT Journal
LA English
CC 3-4 (Biochemical Genetics)
Section cross-reference(s): **16**
AB A thermostable lipase gene from Pseudomonas fluorescens SIK W1 was

overexpressed in Escherichia coli BL21 using expression vector pTTY2. The amount of lipase produced by E. coli BL21 with pTTY2 was more than **40%** of the total cell **proteins** when induced with isopropyl-β-D-thiogalactopyranoside. The lipase was produced as inclusion bodies in the cytoplasm of E. coli. They were solubilized by 8 M urea and refolded into biol. active form. The refolding lipase showed high thermostability; the time required for 90% inactivation of the enzyme (D-value) was 4 h at 95° and the increment of **temperature** to reduce **heating** times by 90% (zD value) was 76. **degree**..

ST Pseudomonas thermostable lipase gene overexpression Escherichia; Escherichia lipase Pseudomonas inclusion body solubilization

IT Escherichia coli
(cloning and overexpression in, of thermostable lipase gene from Pseudomonas fluorescens, inclusion body formation and solubilization in relation to)

IT Gene and Genetic element, microbial
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(for thermostable lipase, of Pseudomonas fluorescens, overexpression in Escherichia coli of)

IT **Heat, biological effects**
(lipase resistant to, of Pseudomonas fluorescens, overexpression in Escherichia coli of)

IT Molecular cloning
(of thermostable lipase gene from Pseudomonas fluorescens, in Escherichia coli)

IT **Solubilization**
(of thermostable lipase of Pseudomonas fluorescens produced as inclusion bodies in Escherichia coli, refolding after)

IT Plasmid and Episome
(pTTY2, for overexpression of thermostable lipase gene of Pseudomonas fluorescens, in Escherichia coli)

IT Pseudomonas fluorescens
(thermostable lipase gene of, overexpression in Escherichia coli of, inclusion body formation and solubilization in relation to)

IT Inclusion bodies
(Pseudomonas fluorescens gene-encoded thermostable lipase produced as, in Escherichia coli, solubilization and refolding in relation to)

IT 9001-62-1, Lipase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(overexpression of gene for thermostable, from Pseudomonas fluorescens, in Escherichia coli)

L84 ANSWER 27 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1991:183796** HCAPLUS
DN **114:183796**
ED Entered STN: 17 May 1991
TI Yeast fermentation processes for insulin production
AU **Diers, Ivan V.**; Rasmussen, Eigil; Larsen, Per Henrik; Kjaersig, Inge Lise
CS **Novo Nordisk** A/S, Bagsvaerd, Den.
SO Bioprocess Technology (**1991**), 13(Drug Biotechnol. Regul.), 166-76
CODEN: BPTEEP; ISSN: 0888-7470
DT Journal
LA English
CC 16-2 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 2, 3

AB Novo Nordisk Co. (Denmark) has devised a biosynthetic production method for human insulin, wherein baker's yeast is utilized to secrete an insulin precursor mol. that is easily recovered from a supernatant containing very few impurities. The genetic construction is tied to the growing cell by a

deletion of the triose phosphate isomerase gene on the chromosome. This host-vector system, developed by ZymoGenetics Inc., Seattle, Washington, has proved extremely stable, and the authors have succeeded in adapting it to a full-scale industrial continuous fermentation process that routinely runs for 3-wk periods.

ST human insulin fermn recombinant yeast

IT **Fermentation**
(human insulin, by recombinant yeast)

IT Saccharomyces cerevisiae
(recombinant, human insulin production by)

IT 9004-10-8P, Insulin, preparation
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, of human by recombinant yeast)

L84 ANSWER 28 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1990:117395** HCAPLUS
DN **112:117395**
ED Entered STN: 31 Mar 1990
TI Effect of pH and **temperature** on cytokine production
PA EGIS Gyogyszergyar, Hung.
SO Ger. Offen., 3 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM C07K015-06
ICS C07K015-26
CC 16-6 (**Fermentation** and Bioindustrial Chemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3907114	A1	19890914	DE 1989-3907114	19890306 <--
	DE 3907114	C2	19911219		
	HU 50218	A2	19891228	HU 1988-1049	19880304 <--
	HU 202594	B	19910328		
	CN 1036794	A	19891101	CN 1989-102021	19890303 <--
	JP 01281095	A2	19891113	JP 1989-50209	19890303 <--
	JP 07024595	B4	19950322		
	AT 8900481	A	19901115	AT 1989-481	19890303 <--
	AT 392800	B	19910610		
PRAI	HU 1988-1049	A	19880304 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 3907114	ICM	C07K015-06
	ICS	C07K015-26

AB In a method for cytokine preparation, the induction and production steps are carried out under different pH and **temp** conditions. This procedure maximizes the yield of cytokines by preventing the action of cytokine synthesis inhibitors during the production step. Thus, simultaneous production of γ-interferon and **interleukin** 2 by human buffy coat leukocytes was induced with Con A at pH 7.2-7.4 and 37.**degree**.. Three h later the pH was adjusted to 7 and the **temperature** to 30. **degree**.. The yield after incubation (15,000 IU γ-interferon/mL and 1300 IU **interleukin** 2/mL) was 2-2.5-fold that obtained at constant **temperature** and unbuffered pH.

ST cytokine formation **temp** pH; interferon formation **temp** pH; **interleukin** 2 formation **temp** pH

IT Leukocyte
(cytokine formation by, of human, pH and **temperature** effect on)

IT Lipocortins
RL: FORM (Formation, nonpreparative)
(formation of, by leukocyte of human, pH and **temperature** effect on)

IT Lymphokines and Cytokines
RL: FORM (Formation, nonpreparative)
(formation of, pH and **temperature** effect on)
IT **Cold, biological effects**
Heat, biological effects
(on cytokine formation, by leukocyte of human)
IT **Lymphokines and Cytokines**
RL: FORM (Formation, nonpreparative)
(**interleukin 2**, formation of, by leukocyte of human, pH and **temperature** effect on)
IT Interferons
RL: FORM (Formation, nonpreparative)
(α, formation of, by leukocyte of human, pH and **temperature** effect on)
IT Interferons
RL: FORM (Formation, nonpreparative)
(γ, formation of, by leukocyte of human, pH and **temperature** effect on)

L84 ANSWER 29 OF 29 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1987:3867** HCAPLUS
DN **106:3867**
ED Entered STN: 11 Jan 1987
TI **Interleukin**-2 production
IN Kitano, Kazuaki; Fujimoto, Shigeru
PA Takeda Chemical Industries, Ltd., Japan
SO Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C12N015-00
ICS C12P021-02
CC 16-4 (**Fermentation** and Bioindustrial Chemistry)
Section cross-reference(s): 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 194818	A2	19860917	EP 1986-301626	19860307	<--
	EP 194818	A3	19880518			
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
	JP 61205497	A2	19860911	JP 1985-48698	19850311	<--
	JP 06046957	B4	19940622			
	DK 8601049	A	19860912	DK 1986-1049	19860307	<--
	CN 86101353	A	19860910	CN 1986-101353	19860310	<--
	CN 1006903	B	19900221			
	ES 552846	A1	19870416	ES 1986-552846	19860310	<--
	US 4935356	A	19900619	US 1989-302064	19890124	<--
PRAI	JP 1985-48698	A	19850311	<--		
	US 1986-835765	B1	19860227	<--		
	US 1988-185307	B1	19880420	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 194818	ICM	C12N015-00
	ICS	C12P021-02
JP 61205497	ECLA	C07K014/55 <--

AB An improved method for producing **interleukin** 2 involves cultivating Escherichia coli transformed with an expression plasmid carrying sequences encoding amino acids 1-133 of **interleukin** 2 at pH 4.8-6.0, preferably 5.5. Expression plasmid pTF4 carrying a human **interleukin** 2 structural gene was used to transform E. coli PR13. A strain which possesses a high **interleukin** 2 productivity (C-4) was selected at pH 7.0. E. coli C-4 was cultured in broth at pH values

ranging 4.5-7.5. The cultures were first grown at 37°; when the growth level reached 500 klett units, the **temperature** was lowered to 30°, and was further lowered to 25. **degree.** at a growth level of 1000 klett units. The total culture time was 24 h. The **interleukin**-2 production at pH 4.8-6 was increased 3-7.5-fold over that obtained in constant **temperature** culture at 37°, pH 7.0.

ST **interleukin** 2 fermn Escherichia pH; **temp** pH
interleukin 2 fermn

IT Escherichia coli
(**interleukin** 2 manufacture with, culture pH and **temperature** in relation to)

IT **Fermentation**
(**interleukin** 2, with Escherichia coli, pH and **temperature** in relation to)

IT **Cold, biological effects**
(on **interleukin** 2 manufacture, with Escherichia coli)

IT **Lymphokines and Cytokines**
RL: BIOL (Biological study)
(**interleukin 2**, manufacture of recombinant, with Escherichia coli, culture pH and **temperature** in relation to)

=> sel hit rn l84
E85 THROUGH E94 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 10:34:18 ON 02 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 MAR 2005 HIGHEST RN 840454-17-3
DICTIONARY FILE UPDATES: 1 MAR 2005 HIGHEST RN 840454-17-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s e85-e94 and l5-l26
1 9004-10-8/BI
(9004-10-8/RN)
1 11061-68-0/BI
(11061-68-0/RN)
1 130391-54-7/BI
(130391-54-7/RN)
1 141732-76-5/BI
(141732-76-5/RN)
1 204521-68-6/BI
(204521-68-6/RN)
1 698973-76-1/BI
(698973-76-1/RN)

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             1 698973-77-2/BI
               (698973-77-2/RN)
             1 89750-14-1/BI
               (89750-14-1/RN)
             1 89750-15-2/BI
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               OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR
               L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR
               L25 OR L26)

=> d ide can tot

L85  ANSWER 1 OF 10  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   698973-77-2  REGISTRY
CN   Proinsulin (synthetic human isoform yMaUJ95) (9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   SCI 13
FS   PROTEIN SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation)

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               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE   1:  141:22295

L85  ANSWER 2 OF 10  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   698973-76-1  REGISTRY
CN   Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-
     L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-
     phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-
     L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-
     L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-
     tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI)  (CA INDEX
     NAME)
FS   PROTEIN SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE   1:  141:22295
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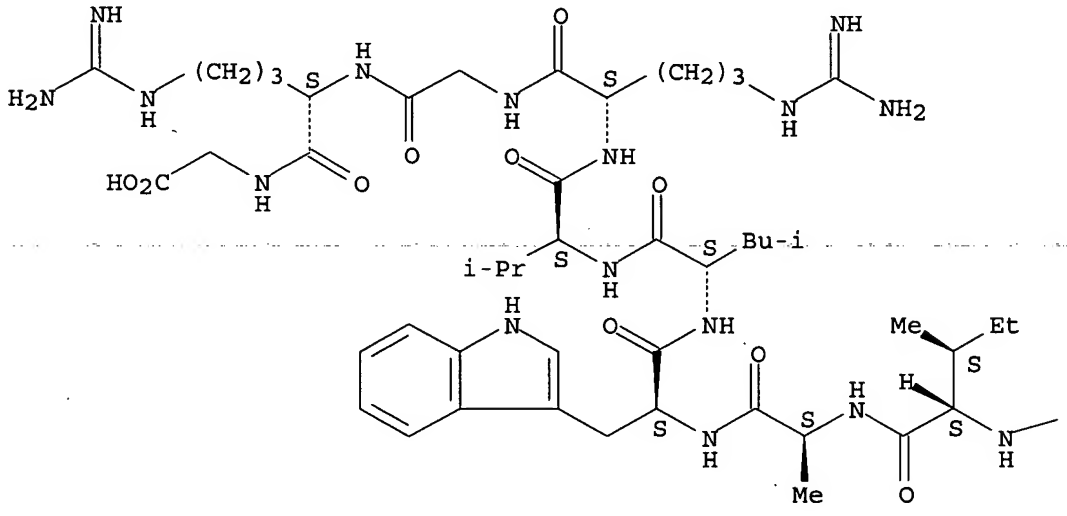
L85 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN **204521-68-6** REGISTRY
CN 7-36-Glucagon-like peptide 1 (Octodon degus), 34-L-arginine-36a-glycine- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7-36-Glucagon-related peptide 1 (Octodon degus), 34-L-arginine-36a-glycine-
OTHER NAMES:
CN 17: PN: WO03010185 TABLE: 1 claimed sequence
CN 17: PN: WO2004069314 PAGE: 21 claimed protein
CN 18: PN: WO0247716 PAGE: 59 claimed protein
CN 242: PN: WO2004005342 PAGE: 46 claimed protein
CN 52: PN: WO03010186 TABLE: 1 claimed protein
CN Arg34-GLP-1(7-37)OH
CN Arg34GLP-1(7-34)
CN Human Arg34GLP-1(7-37)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C151 H228 N42 O47
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: RACT (Reactant or reagent)

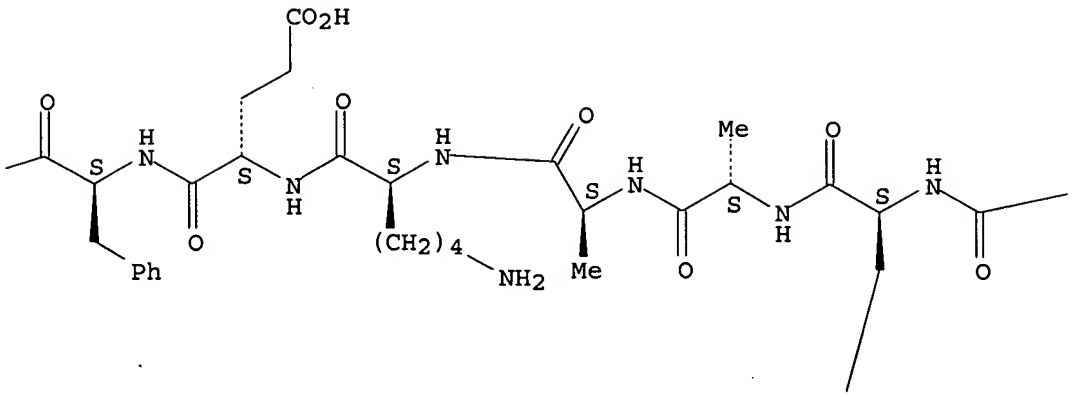
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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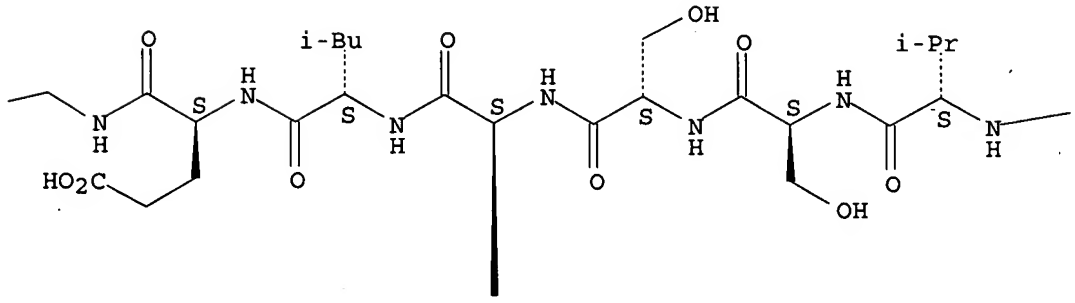
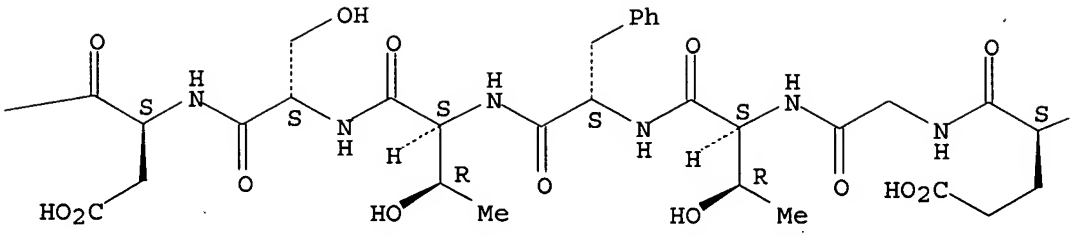


PAGE 1-D



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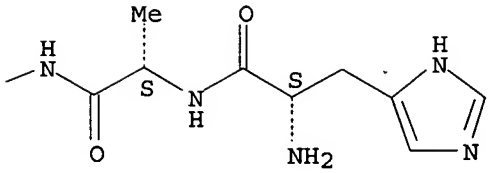

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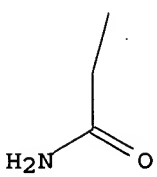

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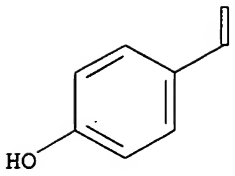

17 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
17 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:362752

REFERENCE 2: 141:212849

REFERENCE 3: 141:22295

REFERENCE 4: 140:105831

REFERENCE 5: 140:5285

REFERENCE 6: 138:149946

REFERENCE 7: 138:149945

REFERENCE 8: 138:78481

REFERENCE 9: 137:42097

REFERENCE 10: 135:273221

L85 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN **141732-76-5** REGISTRY
CN Exendin 4 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 18: PN: WO2004069314 PAGE: 21 claimed protein
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

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219 REFERENCES IN FILE CA (1907 TO DATE)
27 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
220 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:170088

REFERENCE 2: 142:148369

REFERENCE 3: 142:130334

REFERENCE 4: 142:128444

REFERENCE 5: 142:100329

REFERENCE 6: 142:86996

REFERENCE 7: 142:79750

REFERENCE 8: 142:62690

REFERENCE 9: 142:62602

REFERENCE 10: 142:33307

L85 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN **130391-54-7** REGISTRY
CN Exendin 3 (9CI) (CA INDEX NAME)
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, EMBASE, MEDLINE, MRCK*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
32 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
32 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:100329

REFERENCE 2: 141:100447

REFERENCE 3: 141:22295

REFERENCE 4: 141:18132

REFERENCE 5: 141:17632

REFERENCE 6: 140:363055

REFERENCE 7: 140:363053

REFERENCE 8: 140:317698

REFERENCE 9: 140:157460

REFERENCE 10: 140:123175

L85 ANSWER 6 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN **89750-15-2** REGISTRY
CN Glucagon-like peptide II (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glucagon-related peptide II
OTHER NAMES:
CN Glucagon-like peptide 2
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CIN, IPA, MRCK*, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
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RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
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299 REFERENCES IN FILE CA (1907 TO DATE)
28 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
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REFERENCE 1: 142:170208

REFERENCE 2: 142:151547

REFERENCE 3: 142:141240

REFERENCE 4: 142:133707

REFERENCE 5: 142:130334

REFERENCE 6: 142:107517

REFERENCE 7: 142:107410

REFERENCE 8: 142:107396

REFERENCE 9: 142:86774

REFERENCE 10: 142:69377

L85 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN **89750-14-1** REGISTRY
CN Glucagon-like peptide I (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glucagon-related peptide I
OTHER NAMES:
CN GLP 1
CN Glucagon-like peptide 1
CN Glucagon-related peptide 1
MF Unspecified
CI COM, MAN
LC STN Files: AGRICOLA, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CIN, EMBASE, IPA, MEDLINE, MRCK*, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
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1399 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:183226

REFERENCE 2: 142:175954

REFERENCE 3: 142:170320

REFERENCE 4: 142:170216

REFERENCE 5: 142:170215

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REFERENCE 7: 142:170213

REFERENCE 8: 142:170212

REFERENCE 9: 142:170209

REFERENCE 10: 142:170208

L85 ANSWER 8 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN **11061-68-0** REGISTRY
CN **Insulin (human) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3,4,44,45,90,91-Hexathia-8,11,14,17,20,23,26,29,32,35,38,41,48,51,54,57,60,63,66,69,72,75,78,81,84,86-hexacosaazabicyclo[72.11.7]dononacontane, cyclic peptide deriv.
CN Insulin (ox), 8A-L-threonine-10A-L-isoleucine-30B-L-threonine-
OTHER NAMES:
CN 6: PN: WO0050456 SEQID: 1-19 claimed protein
CN H-Tronin
CN Human Insulatard
CN **Human insulin**
CN Human Protaphane
CN Humulin
CN Humulin N
CN Humulin N-U 100
CN Humulin R
CN Humulin S
CN Insulin (Cercopithecus aethiops)
CN Insulin (Macaca fascicularis)
CN Insulin (Macaca mulatta)

CN Insulin (Pan troglodytes)
CN Isuhuman
CN L-Threonine, L-phenylalanyl-L-valyl-L-asparaginyl-L-glutaminyl-L-histidyl-L-leucyl-L-cysteinylglycyl-L-seryl-L-histidyl-L-leucyl-L-valyl-L-α-glutamyl-L-alanyl-L-leucyl-L-tyrosyl-L-leucyl-L-valyl-L-cysteinylglycyl-L-α-glutamyl-L-arginylglycyl-L-phenylalanyl-L-phenylalanyl-L-tyrosyl-L-threonyl-L-prolyl-L-lysyl-, cyclic (7→7'),(19→20')-bis(disulfide) with glycyl-L-isoleucyl-L-valyl-L-α-glutamyl-L-glutaminyl-L-cysteinyl-L-cysteinyl-L-threonyl-L-seryl-L-isoleucyl-L-cysteinyl-L-seryl-L-leucyl-L-tyrosyl-L-glutaminyl-L-leucyl-L-α-glutamyl-L-asparaginyl-L-tyrosyl-L-cysteinyl-L-asparagine cyclic (6'→11')-disulfide
CN Novolin
CN Novolin ge Toronto
CN Novolin R
CN Penfil R
CN Ultraphane
CN Umulin
CN Velosuline HM
FS PROTEIN SEQUENCE
MF C257 H383 N65 O77 S6
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
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RELATED SEQUENCES AVAILABLE WITH SEQLINK

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642 REFERENCES IN FILE CA (1907 TO DATE)
93 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
644 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:183424

REFERENCE 2: 142:148892

REFERENCE 3: 142:86648

REFERENCE 4: 142:62463

REFERENCE 5: 142:33080

REFERENCE 6: 142:23499

REFERENCE 7: 142:11479

REFERENCE 8: 141:400973

REFERENCE 9: 141:366463

REFERENCE 10: 141:314620

L85 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN **9007-92-5** REGISTRY
CN Glucagon (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Glucagonoid
CN Glukagon
CN HG-Factor
CN HGF
CN Hyperglycemic-glycogenolytic factor
DR 12709-67-0, 37307-57-6, 37328-81-7, 82905-30-4
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, NIOSHTIC, PHAR, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

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16209 REFERENCES IN FILE CA (1907 TO DATE)
236 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
16218 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 142:183446

REFERENCE 2: 142:183424

REFERENCE 3: 142:183226

REFERENCE 4: 142:176013

REFERENCE 5: 142:176007

REFERENCE 6: 142:172936

REFERENCE 7: 142:170423

REFERENCE 8: 142:170322

REFERENCE 9: 142:170214

REFERENCE 10: 142:169663

L85 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN
RN **9004-10-8** REGISTRY
CN Insulin (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Actrapid
CN Actrapid HM
CN Actrapid MC
CN Decurvon
CN Dermulin
CN Endopancrine
CN Exubera
CN HMR 4006
CN Iletin
CN Insular
CN Insulin Injection
CN Insulyl
CN Intesulin B
CN Iszilin
CN Mixtard
CN Musulin
DR 8049-67-0, 8049-95-4, 9004-12-0, 9037-76-7, 9045-63-0, 9045-65-2, 9045-66-3, 9045-67-4, 9066-39-1, 9066-40-4, 11081-38-2, 57126-42-8, 37243-75-7, 37294-43-2, 69090-47-7, 88026-11-3, 88026-12-4
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT

(Reactant or reagent); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

101453 REFERENCES IN FILE CA (1907 TO DATE)
1854 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
101587 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:183587

REFERENCE 2: 142:183488

REFERENCE 3: 142:183474

REFERENCE 4: 142:183473

REFERENCE 5: 142:183446

REFERENCE 6: 142:183445

REFERENCE 7: 142:183424

REFERENCE 8: 142:183242

REFERENCE 9: 142:183226

REFERENCE 10: 142:183187

=> d his

(FILE 'HOME' ENTERED AT 09:11:53 ON 02 MAR 2005)
SET COST OFF

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E MARKUSSEN J/AU
L2 124 S E3-E6
E DIERS I/AU
L3 33 S E3-E6
L4 2723 S (NOVO(L)NORDISK?)/PA,CS
SEL RN L1

FILE 'REGISTRY' ENTERED AT 09:17:24 ON 02 MAR 2005
L5 10 S E1-E10
L6 9 S L5 NOT ETHANOL/CN
E INSULIN/CN
E INSULIN (HUMAN)/CN
L7 1 S E3
L8 4024 S INSULIN (L) HUMAN
L9 3121 S L8 AND PROTEIN/FS
L10 1911 S L9 AND INSULIN()HUMAN/INS.HP
L11 1210 S L9 NOT L7,L10
L12 377 S L11 NOT INSULIN LIKE GROWTH FACTOR
L13 353 S L12 NOT INSULIN LIKE
L14 350 S L13 NOT ENZYME
L15 299 S L14 NOT GENE
L16 293 S L15 NOT INSULIN RESPONSIVE
L17 293 S L16 NOT DNA
L18 226 S L17 AND INSULIN/INS.HP
L19 217 S L18 NOT KINASE

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L20          214 S L19 NOT CCS/CI
L21          212 S L20 NOT ANTI INSULIN
L22          209 S L21 NOT INSULIN PROMOTER
L23          179 S L22 NOT FUSION PROTEIN
L24          178 S L23 NOT INSULINASE
L25         7545 S INSULIN NOT L6,L7,L24
L26         5905 S L25 NOT NUCLEIC/FS

     FILE 'HCAPLUS' ENTERED AT 09:32:54 ON 02 MAR 2005
                  E FERMENTATION/CT
L27         5515 S E7,E9,E15
                  E E3+ALL
L28        91162 S E4+NT
                  E FERMENTATION/SC,SX
L29       150611 S E3,E4
L30       202504 S FERMENT?/SC,SX
L31       217709 S L27-L30
                  E TEMPERATURE/CT
L32          602 S E3-E6,E9 AND L31
                  E E3+ALL
L33          765 S E1+NT AND L31
                  E E57+ALL
L34          606 S E1+NT AND L31
                  E E12+ALL
L35          347 S E7+NT AND L31
                  E E33+ALL
L36           41 S E1+NT AND L31
                  E TEMPERATURE/CT
L37            0 S E13+NT AND L31
L38         2192 S E21+NT AND L31
L39         3875 S L32-L38
                  E COOL/CT
L40           72 S E33,E35 AND L31
                  E E33+ALL
L41          477 S E7+NT AND L31
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                  E E6+ALL
L43          899 S E6+NT AND L31
L44         4359 S L39-L43
                  E PRECEIPATATION/CT
                  E PRECIPATATION/CT
                  E PRECIPITATION/CT
L45            0 S E3 AND L44
L46            0 S E25 AND L44
L47            0 S E23 AND L44
                  E E5+ALL
L48           74 S E3,E4,E2+NT AND L44
                  E E38+ALL
L49            0 S E1 AND L44
                  E SULUBILITY/CT
                  E SOLUBILITY/CT
L50           39 S (E3+OLD,NT OR E7+OLD,NT OR E8 OR E9+OLD,NT OR E16+OLD,NT) AND
L51            8 S L48 AND L50
L52           12 S L6,L7,L24 AND L44
L53            6 S L26 AND L44
L54           16 S L52,L53
L55           30 S L2,L3 AND L31
L56            1 S L55 AND L44
L57           29 S L55 NOT L56
                  SEL DN AN 19
L58            1 S L57 AND E1-E3
L59            8 S PEPTIDE#/CW (L) TFF
L60            1 S L44 AND (TREFOIL FACTOR FAMILY OR TFF OR L59)
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                E INTERLEUKINS/CT
                E E3+ALL
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                E ALBUMIN/CT
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                E E46+ALL
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L64           3 S L54,L61,L63 AND L48,L50
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L69          83 S L68 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L70          78 S L69 AND (DEGREE OR TEMPERATURE OR HEAT? OR COOL? OR THERMAL?
L71           5 S L69 NOT L70
                SEL DN AN 3
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L73          45 S L70 AND (?PROTEIN? OR ?PEPTIDE?)
L74          49 S L70 AND (?INSULIN? OR EXENDIN OR GLUCAGON OR TFF OR TREFOIL F
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L76          18 S L70 NOT L75
                SEL DN AN 1 3 7 10 14
L77           5 S L76 AND E4-E18
L78           9 S L75 AND 60
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L79           3 S L78 NOT E19-E36
L80          51 S L75 NOT L76-L79
L81           4 S L80 AND 40
L82          47 S L80 NOT L81
                SEL DN AN 5 6 9 10 13 15 17 20 21 24 31 33 35 38 43 45
L83          16 S E37-E84 AND L82
L84          29 S L72,L77,L79,L81,L83 AND L1-L4,L27-L83

     FILE 'HCAPLUS' ENTERED AT 10:33:38 ON 02 MAR 2005
                SEL HIT RN L84

     FILE 'REGISTRY' ENTERED AT 10:34:18 ON 02 MAR 2005
L85          10 S E85-E94 AND L5-L26

=> => fil wpix
FILE 'WPIX' ENTERED AT 11:29:30 ON 02 MAR 2005
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FILE LAST UPDATED:          28 FEB 2005      <20050228/UP>
MOST RECENT DERWENT UPDATE:     200514        <200514/DW>
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=> d all abeq tech abex tot

L131 ANSWER 1 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2004-707273 [69] WPIX
DNC C2004-249390
TI Method of selectively collecting N-terminal peptide fragment of protein, by protecting amino groups of target protein, cleaving protected protein into N-terminal peptide fragment and other fragments, separating N-terminal peptide fragment.
DC A96 B04 D16
IN ANDO, E; NAKAZAWA, T; NORIOKA, S; OKAMURA, T; UEYAMA, N; YAMAGUCHI, M
PA (SHMA) SHIMADZU CORP; (ANDO-I) ANDO E; (NAKA-I) NAKAZAWA T; (NORI-I) NORIOKA S; (OKAM-I) OKAMURA T; (UEYA-I) UEYAMA N; (YAMA-I) YAMAGUCHI M
CYC 2
PI US 2004152155 A1 20040805 (200469)* 25 C12P021-06 <--
JP 2004219412 A 20040805 (200457) 31 G01N030-88
ADT US 2004152155 A1 US 2003-739111 20031219; JP 2004219412 A JP 2003-426478 20031224
PRAI **JP 2002-375399 20021225**
IC ICM **C12P021-06**; G01N030-88
ICS **C07K001-16**; **C07K001-22**; G01N030-06; G01N030-08; G01N030-48; G01N033-50
AB US2004152155 A UPAB: 20041027
NOVELTY - Selectively collecting (M1) N-terminal peptide fragment of a protein comprising a step of protecting side chain-amino groups of amino acid residues of protein of interest, step of cleaving protected protein into N-terminal peptide fragment (F1) having N-terminus of the peptide of interest, and peptide fragments (F2), and a step of separating F1 from F2 by eluting F1 based on difference in their affinity to substrate, is new.

DETAILED DESCRIPTION - Selectively collecting (M1) the N-terminal peptide fragment of a protein, involves:

(a) protecting side chain-amino groups of amino acid residues containing side chain-amino groups of a protein of interest, to obtain a protected protein protected on the side chain-amino groups; a fragmentation step of cleaving the protected protein into one N-terminal peptide fragment (F1) containing the N-terminus of the peptide of interest, and one or more peptide fragments (F2) other than F1; and a step of separating F1 from F2 by selectively eluting F1 based on the difference in their reactivity or affinity to substrate, where the selective elution is achieved either by allowing F2 to bind to the substrate while allowing F1 to elute, or by allowing F1 to bind to the substrate while allowing F2 to elute and subsequently eluting the bound F1; or

(b) a fragmentation step of cleaving a protein of interest into one N-terminal peptide fragment (F3) and one or more peptide fragments (F4) other than F3; step of protecting side chain-amino groups of amino acid residues containing side chain-amino group of F3 and F4 to obtain F1 protected on the side chain-amino groups, along with the F2 protected on the side chain-amino groups, and performing the separation step of (a).

USE - (M1) is useful for selectively collecting the N-terminal peptide fragment of a protein (claimed). The N-terminal peptide fragment obtained by (M1) is useful in determining protein amino acid sequence.

ADVANTAGE - (M1) enables selective method for collecting N-terminal

peptide fragments of a protein of interest whether or not the protein of interest is modified on the N-terminus, thus allowing the sequencing of protein of interest from the N-terminus, by mass-spectrometry-based protein sequencing.

Dwg.1/10

FS CPI

FA AB; GI; DCN

MC CPI: A12-L04; A12-V00V; B04-B04C2; B04-G01; **B04-N04**; B04-N06; B11-B; B12-K04; D05-H11; **D05-H13**

TECH UPTX: 20041027

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The step (a) of (M1) involves step of guanidinating side chain-amino groups of amino acid residues containing side chain-amino groups of a protein of interest, to obtain a guanidinated protein in which the side chain-amino groups have been converted to guanidine groups, and the fragmentation step of cleaving the guanidinated protein into F1 and one or more F2. The step (b) of (M1) involves fragmentation step of cleaving a protein of interest into F3 and one or more F4, and a protection step of guanidinating side chain-amino groups of amino acid residues containing side chain-amino groups of F3 and F4, to obtain a guanidinated F1 in which the side chain-amino groups have been converted to guanidino groups, along with F2 in which the side chain-amino groups have been converted to guanidino groups. The protein of interest is a protein modified on the N-terminus, and the separation step is achieved by allowing F2 to bind to the substrate while allowing F1 to elute. The substrate comprises a molecule or portion of molecule that can chemically react with an amino group to form a covalent bond. The substrate is chosen from p-phenylene diisothiocyanate (DITC) polymer resin and allylamine polymer resin. (M1) further involves after fragmentation step or the guanidination step and before the separation step, a step of coupling an affinity compound with the N-terminuses of F2, where the affinity compound is capable of specifically binding to a particular molecule or a particular portion of a molecule to form a complex, and the substrate includes an immobilized ligand comprising the particular molecule or the particular portion of the molecule. The affinity compound is an antigen or biotin derivative, and the ligand is an antibody against the antigen, or avidin.

In (M1), when the protein of interest is a protein with unmodified N-terminus, and the method further involves after the guanidination step and before the fragmentation step, a step of modifying the unmodified N-terminus of the protein of interest., The unmodified N-terminus of the protein of interest is modified with an affinity compound that can specifically bind to a particular molecule or a particular portion of a molecule to form a complex. The substrate comprises an immobilized ligand having the particular molecule or the particular portion of the molecule, and the separation step is achieved by allowing F1 to bind to the substrate while allowing F2 to elute and subsequently eluting the bound F1, or by allowing F2 to bind the substrate while allowing F1 to elute.

ABEX UPTX: 20041027

EXAMPLE - The N-terminal peptide fragment of neurotensin was selectively collected by the following method. Neurotensin (30 microl, 0.67 mM), aqueous ammonia solution (33 microl, 9 N), and o-methylisourea (9 microl, 6 M) were mixed with one another and the reaction was allowed to proceed at 65 **degrees** Centigrade for 30 minutes, and the guanidinated peptide was obtained. The guanidinated neurotensin was subjected to reverse-phase HPLC chromatogram, and the main peak that contained unreacted neurotensin was determined by matrix-assisted laser desorption ionization (MALDI). The main peak fraction was collected and was purified by reverse-phase HPLC. The purified product was dried to form a solid sample. To the sample, a 30 microl trypsin solution (0.1 microg/microl), prepared by adding trypsin to aqueous solution of calcium chloride (5 mM) and ammonium bicarbonate (50 mM) was added. The mixture was left overnight to digest the guanidinated peptide. The digested sample (3.3 microl), Tris-hydrochloric acid buffer (32.7 microl, 100 mM) (pH 8.3), 12.5%

aqueous solution of trimethylamine (4 microl), and acetonitrile (4 microl) were mixed with one another. The mixture was loaded on a p-phenylene diisothiocyanate (DITC) polymer resin column and the reaction was allowed to proceed at **60 degrees** Centigrade for 1 hour. After the reaction, the resin was washed with a mixture (300 microl) of 0.1% trifluoroacetic acid, 2-propanol, and acetonitrile containing the respective components at a volume ratio of 4:3:3. The resulting eluate was collected and was dried to form a solid product. The product was then redissolved in a 0.1% aqueous solution of trifluoroacetic acid and was subjected to analysis by reverse-phase HPLC and MALDI. Thus, the N-terminal peptide fragment of neurotensin was selectively collected.

L131 ANSWER 2 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2004-450393 [42] WPIX
DNC C2004-168821
TI Purifying fermentation-derived product, by **heating** fermentation broth having fermentation-derived product to specific **temperature** , separating precipitate from soluble portion of broth, and isolating fermentation-derived product.
DC B04 D16
IN **DIERS, N; MARKUSSEN, J; DIERS, I**
PA (DIER-I) DIERS I; (MARK-I) MARKUSSEN J; (NOVO) NOVO NORDISK AS
CYC 107
PI WO 2004048588 A1 20040610 (200442)* EN 17 C12P021-00 <--
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
US 2004137571 A1 20040715 (200447) C07K001-14 <--
AU 2003281982 A1 20040618 (200471) C12P021-00 <--
ADT WO 2004048588 A1 WO 2003-DK801 20031124; US 2004137571 A1 **Provisional US 2002-430748P 20021204, US 2003-719601 20031121**; AU 2003281982 A1 AU 2003-281982 20031124
FDT AU 2003281982 A1 Based on WO 2004048588
PRAI **US 2002-430748P 20021204; DK 2002-1821 20021126**
IC ICM **C07K001-14; C12P021-00**
ICS **C07K001-14**
AB WO2004048588 A UPAB: 20040702
NOVELTY - Purifying (M1) a fermentation-derived product, involves:
(1) **heating** the fermentation broth (I) containing the fermentation-derived product or its precursor to a **temperature** of **60**-90 **deg.** C,
(2) **cooling** (I) to a **temperature** below **60 deg.** C,
(3) separating the precipitate from the soluble portion of (I) at a **temperature** less than **60 deg.** C, and
(4) isolating the fermentation-derived product.
USE - (M1) is useful for purifying a fermentation-derived product. The fermentation-derived product or its precursor is a protein, which is a pharmaceutical protein or a precursor. The protein is chosen from GLP-1, exendin-4, exendin-3, GLP-2, glucagon, TFF peptides, interleukins, insulin, albumin, human insulin, human insulin precursor, human insulin analog, human insulin analog precursor, Arg34-GLP-1(7-37), and Glu-Glu-Ala-Glu-Lys-Arg34-GLP-1(7-37) (claimed).
ADVANTAGE - (M1) allows precipitating and removing impurities from culture broth. (M1) enables continuous industrial manufacture of fermentation-derived products, and better separation of products and impurities. (M1) reduces manufacturing costs and down-time of chromatographic columns during separation of fermentation-derived

products.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: **B04-C01**; **B04-H02**; **B04-J03A**; **B04-J03B**; **B04-N02**; **B04-N04**; D05-C12; **D05-H13**; D05-H14A1; D05-H14A2
TECH UPTX: 20040702
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (M1), flocculation agent is not added to (I). The soluble portion of (I) in step (c) contains at least **60**% of the product, which results in the fermentation-derived product in step (d). The mean residence time of (I) at **temperatures** 60-90 **degreesC** in step (a) is less than **60** minutes, 30 minutes, 15 minutes, most preferably less than 10 minutes. (I) is **cooled** to **temperature** below 35 **degreesC** in step (b). The **temperature** of (I) during the separation step (c) is less than 40 **degreesC**, 35 **degreesC** or 25 **degreesC**, preferably less than 10 **degreesC**. The separation in step (c) is performed by centrifugation or microfiltration.
The steps (a), (b) and (c) are run in continuous mode. The soluble portion of (I) produced in step (c) is subjected to column chromatography, crystallization, precipitation or ultrafiltration, where the cut-off value of the ultrafiltration membrane is lower than four times the molecular weight of the fermentation-derived product, preferably lower than twice the molecular weight of the fermentation-derived product, and most preferably lower than the molecular weight of the fermentation-derived product. The product containing fluid resulting from ultrafiltration is subjected to column chromatography.
(M1) further involves cultivating recombinant host cells to produce (I). The host cells are chosen from Escherichia coli, Saccharomyces cerevisiae, Pichia pastoris, Pichia methanolica, Candida utilis, and Kluyveromyces lactis. The fermentation-derived product or its precursor has a molar weight less than 25000 Dalton, 10000 Dalton or 7000 Dalton, preferably 4000 Dalton.
ABEX UPTX: 20040702
EXAMPLE - Peptide single chain insulin (SCI)-13 having sequence such as (B-chain)-Gly-Tyr-Gly-Asn-His-Asp-Leu-Asn-Phe-Pro-Gln-Thr-(A-chain) was obtained, where (B-chain) was the 30 amino acid B-chain of human insulin, (A-chain) was 21 amino acid A-chain of human insulin, and the 12 amino acid peptides connected the C-terminus of the B-chain to the N-terminus of the A-chain. Yeast cells transformed with plasmid pMaUJ360 coding for SCI-13, were grown in a 10 L fermentor on YPD-medium with glucose added separately by a linear gradient. After 2 days fermentation 9.35 L of broth was harvested and centrifuged to yield 7.5 L of supernatant. Two liter of supernatant was added to 3 L of ethanol, and the pH was adjusted to 3.0 with dilute hydrochloric acid. The precipitate formed was removed by centrifugation, and 5 ml portions of the clear supernatant were subjected to treatment for 5 minutes at **60**, 80 and 93degreesC, respectively. The amount of free SCI-13 in the samples was estimated by the following high performance layer chromatography (HPLC) analysis. A4x150 mm column of C-18 5 mu was used and the effluent was analyzed by UV-detection at 214 nm. A linear gradient from 90% buffer A (0.018 M ammonium sulfate, 0.0125 M Tris, 20% CH3CN, pH 7.0) and 10% B (50% CH3CN) to 20% buffer A and 80% B was applied during 20 minutes using a pumping rate of 1.5 ml/min. A standard of human insulin emerges in this system at 12.8 minutes and the SCI-13 compound emerges at 12.1 minutes. Result showed that the impurities were precipitated and the SCI-13 compound was rendered fully soluble by the **heat** treatment of the broth. Thus, the **heat** treatment of the broth resulted in solution, which was conditioned for further purification steps by column chromatography or other processes where it was desirable that the product was in freely soluble form.

L131 ANSWER 3 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2003-820683 [77] WPIX
DNC C2003-231034
TI Collagen peptide for use in foodstuffs, beverages and cosmetics, contains preset amount of free amino acid and arsenic, and is obtained from enzymatic-degraded substance of fish skin and/or bone extract.
DC B04 D13 D16 D21
PA (YAES-N) YAESU SUISAN KAGAKU KOGYO KK
CYC 1
PI JP 2003238597 A 20030827 (200377)* 8 C07K014-78
ADT JP 2003238597 A **JP 2002-37933 20020215**
PRAI **JP 2002-37933 20020215**
IC ICM C07K014-78
ICS A23L001-30; A23L001-305; A61K007-00; A61K007-075; B01D061-02; **C07K001-12**; **C07K001-34**; **C12P021-06**
ICA A21D002-26; A21D013-08; A23L002-38; A23L002-52; A23L002-66
ICI C12R001:91; **C12P021-06**
AB JP2003238597 A UPAB: 20031128
NOVELTY - A collagen peptide comprises 1 mass% or less of free amino acid and 2 parts per million (ppm) or less of arsenic. The peptide is obtained from enzymatic-degraded substance of fish skin and/or bone extract using reverse osmosis membrane.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) manufacture of collagen peptide from fish, which involves extracting collagen from fish skin and/or bone, decomposing the obtained extract using enzymes, followed by concentrating the enzymatic-degraded substance using reverse osmosis membrane and purifying;
(2) foodstuffs/beverages containing the collagen peptide; and
(3) cosmetics containing the collagen peptide.
USE - For use in foodstuffs, beverages and cosmetics.
ADVANTAGE - The collagen peptide has taste and smell that is peculiar to fish. The peptide contains trace amount of arsenic, hence the peptide is highly safe.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-L05C; **B04-N02**; **B04-N04**; B11-B; B11-C08D3; D03-F01; D03-F04; D03-H01T2; D05-A02C; **D05-H13**; D08-B
TECH UPTX: 20031128
TECHNOLOGY FOCUS - BIOLOGY - Preferred Property: The molecular weight of collagen peptide is 1000-10000 daltons.
Preferred Method: The concentration performed using reverse osmosis membrane has salt prevention rate of 10-50%. The method further involves performing de-coloring and deodorizing.
ABEX UPTX: 20031128
EXAMPLE - Water (24 l) was added to 12 kg of cod fish bones and extracted at 95 **degrees** C for 3 hours. The **hot** extract was **cooled**, filtered and adjusted to pH7. Then, 3.6 g of Protease N (protease formulation) was added to the extract and reacted for **60** minutes at **60 degrees** C. Taiko S-W50 (activated carbon) was added to 360 g of the enzyme treated liquid, **heated** for 15 minutes at 80 **degrees** C, **cooled** and filtered to obtain 25 l of filtrate. The filtrate was then passed through reverse membrane to obtain concentrated liquid. The obtained concentrated liquid was spray-dried to obtain 900 g of white collagen peptide powder containing (in mass%) water (6.1), solid (0.1 or less), ash (2.5), fat (0.1 or less), total nitrogen (15.3) and chondroitin sulfate (5.2). Collagen peptide (in weight%) (10), vitamin C (0.6), vitamin B2 (0.01), erythritol (10), acidic flavor (1.2), sweet flavor (suitable quantity), perfume (suitable quantity) and purified water (remaining quantity), were mixed uniformly to obtain a health drink having favorable quantity.

L131 ANSWER 4 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2003-268032 [26] WPIX
DNC C2003-069886
TI Making polypeptides having at least one lysine residue in transformed host cells by expressing a precursor molecule of the desired polypeptide which is to be acylated and subsequently cleaved.
DC B04 D16
IN BALSCHMIDT, P; **DIERS, N**; EGEL-MITANI, M; JONASSEN, I; KJELDSEN, T B; **MARKUSSEN, J**; **DIERS, I**
PA (BALS-I) BALSCHMIDT P; (DIER-I) DIERS I; (EGEL-I) EGEL-MITANI M; (JONA-I) JONASSEN I; (KJEL-I) KJELDSEN T B; (MARK-I) MARKUSSEN J; (NOVO) NOVO NORDISK AS
CYC 101
PI WO 2003010186 A2 20030206 (200326)* EN 42 C07K001-00 <--
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
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US 2003144471 A1 20030731 (200354) A01N037-18
EP 1421103 A2 20040526 (200435) EN C07K001-00 <--
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
KR 2004019361 A 20040305 (200444) C07K007-08
AU 2002355161 A1 20030217 (200452) C07K001-00 <--
BR 2002011346 A 20040921 (200470) C07K001-00 <--
JP 2005504527 W 20050217 (200513) 75 C12P021-02 <--
ADT WO 2003010186 A2 WO 2002-DK502 20020718; US 2003144471 A1 Provisional US 2001-310793P 20010808, US 2002-205110 20020724; EP 1421103 A2 EP 2002-750842 20020718, WO 2002-DK502 20020718; KR 2004019361 A KR 2004-701057 20040120; AU 2002355161 A1 AU 2002-355161 20020718; BR 2002011346 A BR 2002-11346 20020718, WO 2002-DK502 20020718; JP 2005504527 W WO 2002-DK502 20020718, JP 2003-515545 20020718
FDT EP 1421103 A2 Based on WO 2003010186; AU 2002355161 A1 Based on WO 2003010186; BR 2002011346 A Based on WO 2003010186; JP 2005504527 W Based on WO 2003010186
PRAI DK 2001-1141 20010724
IC ICM A01N037-18; **C07K001-00**; C07K007-08; **C12P021-02**
ICS A61K038-00; C07K002-00; C07K014-47; C07K014-605
AB WO2003010186 A UPAB: 20030428
NOVELTY - Making a polypeptide with at least one lysine residue being acylated in its epsilon -amino group, comprising culturing a host cell with a polynucleotide encoding and expressing a precursor molecule, separating the precursor from the culture broth, preferentially acylating the epsilon -amino group in the desired polypeptide, removing the N-terminal extension from the acylated precursor by enzymatic cleavage and isolating the acylated polypeptide, is new.

DETAILED DESCRIPTION - Making a polypeptide with at least one lysine residue being acylated in its epsilon -amino group, comprising culturing a host cell with a polynucleotide encoding and expressing a precursor molecule, separating the precursor from the culture broth, preferentially acylating the epsilon -amino group in the desired polypeptide, removing the N-terminal extension from the acylated precursor by enzymatic cleavage and isolating the acylated polypeptide, is new. The precursor molecule comprises the desired polypeptide and an N-terminal extension cleavable from the desired polypeptide at a lysine cleavage site. Step (c) further comprises not acylating the epsilon -amino group of the lysine cleavage site in the N-terminal extension.

An INDEPENDENT CLAIM is also included for a polypeptide precursor for a desired polypeptide having the formula (A);

N-terminal-extension-Lys-Z3 - Z4 - asterisk polypeptide asterisk (A).

Lys = a cleavage site, the N-terminal extension has 2-14 amino acid

residues and is capable of preventing or minimizing acylation of the Lys cleavage site and protecting the polypeptide precursor against proteolytic degradation during fermentation;

Z3 = His or Tyr and is the N-terminal amino acid residue in the desired polypeptide;

Z4 = the next amino acid residue from the N-terminal end in the desired polypeptide and is Ala, Ser or Gly; and

asterisk polypeptide asterisk = the remaining sequence of the desired polypeptide.

USE - The methods and compositions of the present invention are useful for the production of polypeptides in transformed host cells by expressing a precursor molecule of the desired polypeptide which is to be acylated and subsequently cleaved at a Lys cleavage site in a subsequent in vitro step.

Dwg.0/1

FS CPI

FA AB; DCN

MC CPI: **B04-C01G**; **B04-N04**; **B04-N04A**; D05-C11; D05-H12A; D05-H12D5; D05-H12E; D05-H14; D05-H17

TECH UPTX: 20030428

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The N-terminal extension in the method for making a polypeptide is up to 15 amino adds in length, or is 3-15, 3-12, 3-10, 3-9, 3-8, 3-7, 3-6 or 3-5 amino adds in length. The polypeptide is preferably monoacylated. One or more amino acid residues in the N-terminal extension are capable of establishing a metal ion complex binding site together with one or more amino acid residues in the N-terminal end of the polypeptide, where the N-terminal extension comprises a metal ion binding site derived from the N-terminal end of porcine or human serum albumin, or from the Zn binding site in metalloendopeptidases. The N-terminal extension of the precursor molecule comprises at least one negatively charged amino acid residue which is capable of establishing a salt bridge with the lysine cleavage site N-terminal to the polypeptide, where the N-terminal extension is capable of forming an alpha-helix. The N-terminal extension further comprises a Ca+2 binding enterokinase site from trypsinogen, or a eukaryotic N-glycosylation site. The desired polypeptide is sensitive to proteolytic degradation at its N-terminal end and where the N-terminal extension prevents or minimizes such proteolytic degradation. The desired polypeptide has an Ala or Pro as the second amino acid residue from the N-terminal end, and has a His as the N-terminal amino acid residue. The N-terminal extension comprises at least one histidine residue. One or more histidine residues in the N-terminal extension are positioned 1-4 residues from the lysine cleavage site. The N-terminal extension is any of the following sequences of (S1)-(S35): (S1) Glu-Glu-Ala-His-Lys; (S2) Glu-(Glu-Ala)2-His-Lys; (S3) Glu-(Glu-Ala)3His-Lys; (S4) Glu-Glu-Gly-His-Lys; (S5) Glu-His-Pro-Lys; (S6) Glu-Glu-Gly-Glu-Pro-Lys; (S7) Glu-Glu-His-Cys-Lys; (S8) Glu-Glu-His-His-Lys; (S9) Glu-His-His-His-Lys; (S10) Glu-His-Ala-His-Lys; (S11) Glu-Gly-Ala-His-Lys; (S12) Glu-His-Gly-His-Gly-Lys; (S13) Glu-Glu-Ala-His-Glu-Leu-Lys; (S14) Glu-Glu-Ala-His-Glu-Ile-Lys; (S15) Glu-Glu-Ala-His-Glu-Val-Lys; (S16) Glu-Glu-Ala-His-Glu-Met-Lys; (S17) Glu-Glu-Ala-His-Glu-Phe-Lys; (S18) Glu-Glu-Ale-His-Glu-Tyr-Lys; (S19) Glu-Glu-Ala-His-Glu-Trp-Lys; (S20) Gln-Asp-Ala-His-Lys; (S21) Glu-Glu-Glu-Ala-Trp-His-Trp-Leu-Lys; (S23) Asp-Thr-His-Lys; (S24) Glu-His-His-Gly-His-Gly-Lys; (S25) Asp-Ser-His-Lys; (S26) Gln-Asp-Thr-His-Lys; (S27) Glu-Ala-Glu-Ala-Glu-Ala-Gln-Asp-Thr-His-Lys; (S28) Glu-Ala-Glu-Ala-Glu-Asp-Thr-His-Lys; (S29) Glu-Ala-Gln-Asp-Thr-His-Lys; (S30) Trp-His-Trp-Leu-Lys; (S31) Glu-Glu-Trp-His-Trp-Leu-Lys; (S32) Glu-Glu-Glu-Ala-Glu-Ala-Trp-His-Trp-Leu-Lys; (S33) Glu-Ala-Gln-Asp-Ala-His-Lys; (S34) Glu-Ala-Glu-Ala-Glu-Ala-Gln-Asp-Ala-His; and (S35) Glu-Ala-Glu-Ala-Glu-Ala-Gln-Asp-Ala-His-Lys. The N-terminal extension comprises at least one Glu or Asp, where the Glu or Asp residues are positioned between 1 to 5 residues from the lysine cleavage site, and additionally comprises a Glu-Glu-sequence. The N-terminal extension is

also Glu-Glu-Ala-Glu-Lys, Glu-Glu-Gly-Glu-Pro-Lys, or Glu-Glu-Lys. The N-terminal extension is alternatively from any of the following sequences of (S36)-(S47): (S36) Glu-Glu-Ala-Glu-Ala-Trp-His-Trp-Leu-Lys; (S37) Glu-Glu-Glu-Ala-Trp-His-Trp-Leu-Lys; (S38) Leu-Asp-Gly-Arg-Leu-Glu-Ala-Leu-Lys; (S39) Glu-Glu-Leu-Asp-Gly-Arg-Leu-Glu-Ala-Leu-Lys; (S40) Glu-Glu-Leu-Asp-Ala-Arg-Leu-Glu-Ale-Leu-Lys; (S41) Glu-Glu-Trp-His-Trp-Leu-Lys; (S42) Glu-Glu-Glu-Ala-Glu-Ata-Trp-His-Trp-Leu-Lys; (S43) Glu-Glu-Gly-Asn-Thr-Thr-Pro-Lys; (S44) Glu-Glu-Gly-Asn-Glu-Thr-Glu-Pro-Lys; (S45) Glu-Glu-Gly-Asn-Asp-Thr-Glu-Pro-Lys; (S46) Glu-Glu-Gly-Asn-Thr-Thr-Glu-Pro-Lys; and (S47) Asp-Asp-Asp-Asp-Lys. The N-terminal extension also has formula (B).

Xn----X1-Lys (B)

Lys = a cleavage site; and

Xn----X3 = a peptide sequence from 2-14 amino acid residues in length having the function of preventing or minimizing acylation of the free epsilon-amino group in the Lys cleavage site and having the further function of protecting the expressed precursor polypeptide from endoproteolytic cleavage.

No X is Lys and that at least one X is His or Glu or Asp. The Xn----X3 is of 2-12 amino acid residues in length. In another embodiment Xn----X3 is of 2-10, 2-9, 2-8, 2-7, 2-6, or 2-5 amino acid residues in length, and also contains 2-8 amino acid residues which are His, Glu, Ala, Asp, Gly, or Pro, or contains 4-10 amino acid residues which are Glu, Asp, Ala, His, Trp, Tyr, Ile, Val, Met and Phe, or contains 5-8 amino acid residues that are Glu, Asp, Gly, Asn, Thr, Ser or Pro. The first and second X from the N-terminal end of the N-terminal extension is Glu or Asp. The desired polypeptide is GLP-1 or GLP-2 or their analog or derivative. The polypeptide is GLP-17-37 acylated in position Lys26 and Lys34. The GLP-I analogue is Arg34GLP17-37 acylated in position Lys26. The enzymatic cleavage is conducted by use of a lysine endopeptidase such as the Achromobacter lyticus protease I. The host cell is a yeast cell that is a Saccharomyces cerevisiae cell or a DELTAYPS1 cell. The acylation step is performed in an organic solvent or in a mixture of water and an organic solvent in the presence of metal ions that is Zn, Cu, Co, Ni, Fe, Mg, Mn or Ca. The organic solvent is CH3CN or NMP. The acylation step is conducted at a pH between 7 and 12, preferably between 8 and 11.5 or 9.0 and 10.5. The acylation step is performed at a **temperature** of -5 to 35 **degrees** C, preferably 15-25 **degrees** C.

Preferred Polypeptide Precursor: The N-terminal sequence in the polypeptide precursor is capable of establishing a metal ion complex binding site together with one or more amino acid residues in the N-terminal end of the polypeptide, and the N-terminal extension comprises a metal ion binding site derived from the N-terminal end of albumin, and further comprises a metal ion binding site derived from the Zn binding site in metalloendopeptidases. Additionally, the N-terminal extension comprises at least one amino acid residue which is capable of establishing a salt bridge with the lysine cleavage site. The N-terminal extension is also capable of forming an alpha-helix, and comprises a eukaryotic glycosylation site. The N-terminal extension alternatively comprises at least one histidine residue, or at least one Glu or Asp. The desired polypeptide is GLP-1 or GLP-2 or their analogue or derivative. The polypeptide is GLP-17-37 acylated in position Lys26 and Lys34. The GLP-I analog is Arg34GLP17-37 acylated in position Lys26.

ABEX UPTX: 20030428

WIDER DISCLOSURE - Polynucleotides, vectors, host cells and promoters used in the novel method.

EXAMPLE - No relevant example given.

L131 ANSWER 5 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2003-239418 [23] WPIX
DNC C2003-061515

TI Making acylated polypeptides, comprises culturing a host cell comprising a polynucleotide sequence encoding a precursor molecule of the desired polypeptide under conditions allowing the expression of the precursor molecule.

DC B04 D16

IN BALSCHMIDT, P; **DIERS, N**; EGEL-MITANI, M; HOEG-JENSEN, T; **MARKUSSEN, J**; **DIERS, I**

PA (BALS-I) BALSCHMIDT P; (DIER-I) DIERS I; (EGEL-I) EGEL-MITANI M; (HOEG-I) HOEG-JENSEN T; (MARK-I) MARKUSSEN J; (NOVO) NOVO NORDISK AS

CYC 101

PI WO 2003010185 A2 20030206 (200323)* EN 13 C07K001-00 <--
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
US 2003082671 A1 20030501 (200331) C12P021-06 <--
EP 1421102 A2 20040526 (200435) EN C07K001-00 <--
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
AU 2002355160 A1 20030217 (200452) C07K001-00 <--

ADT WO 2003010185 A2 WO 2002-DK501 20020718; US 2003082671 A1 Provisional US 2001-310952P 20010808, US 2002-205270 20020724; EP 1421102 A2 EP 2002-750841 20020718, WO 2002-DK501 20020718; AU 2002355160 A1 AU 2002-355160 20020718

FDT EP 1421102 A2 Based on WO 2003010185; AU 2002355160 A1 Based on WO 2003010185

PRAI DK 2001-1140 20010724

IC ICM **C07K001-00**; **C12P021-06**
ICS C07K014-605

AB WO2003010185 A UPAB: 20030407
NOVELTY - Making a desired polypeptide comprising at least one lysine residue being acylated in its epsilon -amino group comprises culturing a host cell comprising a polynucleotide sequence encoding a precursor molecule of the desired polypeptide under conditions allowing the expression of the precursor molecule.

DETAILED DESCRIPTION - A method for making a desired polypeptide comprising at least one lysine residue being acylated in its epsilon -amino group, comprising:

(a) culturing a host cell comprising a polynucleotide sequence encoding a precursor molecule of the desired polypeptide under conditions allowing the expression of the precursor molecule, where precursor molecule comprises an N-terminal extension capable of protecting the desired polypeptide against proteolytic degradation and having a cleavage site different from Lys positioned at its C-terminal end for cleavage from the desired polypeptide;

(b) separating the expressed precursor from the culture broth;

(c) acylating the epsilon -amino group of at least one lysine residue in the desired polypeptide;

(d) removing the N-terminal extension by chemical and/or enzymatic cleavage and isolating the acylated polypeptide.

An INDEPENDENT CLAIM is also included for a polypeptide precursor for a desired polypeptide, where the precursor has the formula (I).

Y = Met, Asn, Pro, Gln, Cys or Arg-Arg;

N-terminal extension = 1-14 amino acid residues; and

polypeptide = the remaining part of the desired polypeptide.

USE - The method is useful for producing acylated proteins or polypeptides.

Dwg.0/1

FS CPI

FA AB; GI; DCN

MC CPI: B04-C01B; B04-F0100E; B04-N04B0E; D05-H14; D05-H17

TECH UPTX: 20030407

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The acylating step is conducted after the removal step, where the polypeptide is monoacylated. The N-terminal extension is up to 15 amino acid residues in length, such as 1-15, 2-15, 3-15, 3-12, 3-10, 3-9, 3-8, 3-7, 3-6 or 3-5 amino acid residues in length. The desired polypeptide belongs to the growth hormone releasing factor (GRF) family of peptides having a His or Tyr in the N-terminal position and Ser, Ala or Gly in the next position, preferably a His-Ala, His-Gly, His-Ser or Tyr-Ala as the N-terminal sequence. The desired polypeptide is GLP-1, GLP2, GLP-1 or GLP-2 analogue, is preferably Arg34GLP1(7-37) acylated in position Lys26. The cleavage site in the N-terminal extension is selected from Met, Asn, Pro, Gln, Cys and Arg-Arg, and comprises a Glu-Glu sequence at the N-terminal end.

The N-terminal extension has the sequence (II):

Xn-------X1 = a peptide sequence of 1-14, preferably 2-14 amino acid residues in length;

Xn-------X1-Y = protects the expressed polypeptide endoproteolytic cleavage, prevents acylation of the N-terminal end of the desired polypeptide and prevents precipitation caused by fibrillation during fermentation, downstream separation and purification steps; and

Y = Met, Asn, Pro, Gln, Cys or Arg-Arg.

The N-terminal extension is selected from:

(a) Glu-Glu-Met;
(b) Glu-Glu-Ala-Glu-Met;
(c) Glu-Glu-Ala-Glu-Asn;
(d) Glu-Glu-Ala-Glu-Arg-Arg;
(e) Gln;
(f) Glu-Pro-Gln;
(g) Glu-Ala-Gln;
(h) Glu-Ala-Glu-Ala-Gln;
(i) Glu-Ala-Glu-Ala-Glu-Ala-Gln;
(j) Glu-Glu-Gly-Cys-Thr-Ser-Ile-Cys;
(k) Glu-His-Gly-Cys-Thr-Ser-Ile-Cys;
(l) Glu-Glu-Ala-Arg-Met;
(m) Glu-Glu-Arg-Asn;
(n) Glu-Glu-Ala-Glu-Asn;
(o) Glu-Glu-Arg-Ala-Arg-Arg;
(p) Glu-Glu-Ala-Glu-Pro;
(q) Glu-Glu-GIy-Glu-Pro;
(r) Glu-Glu-Ala-Glu-Cys; and
(s) Glu-Glu-Ile-Glu-Gly-Arg.

The host cell is a yeast cell, preferably Saccharomyces cerevisiae cell.

Preferred Polypeptide Precursor: The polypeptide precursor has the formula (III):

Y1 = is Met, Asn, Pro, Gln, Cys or Arg-Arg;
Y2 = His or Tyr;
Y3 = Ala, Ser or Gly;
N-terminal extension = 1-14 amino acid residues; and
polypeptide = the remaining part of desired polypeptide, which is GLP-1, GLP-2 or their analogue.

The desired polypeptide is Arg34GLP1(7-37) acylated in position Lys26.

ABEX UPTX: 20030407

WIDER DISCLOSURE - Also disclosed recombinant host cells comprising a polynucleotide encoding the precursor molecule.

EXAMPLE - Plasmid pKV304 containing DNA encoding Arg34GLP-197-37) without an N-terminal extension was digested with either EagI+NcoI or EagI+Asp718. After agarose electrophoresis and purification, fragments of 1.4 kb and 10 kb, respectively, were isolated. Oligonucleotide adaptors corresponding to various N-terminal extensions of Arg34GLP-197-37) containing NcoI and Asp718 cleavage sites were also purified. The 1.4 kb fragment (EagI+NcoI), 10 kb fragment (EagI+Asp718) and the adaptor fragment designed for the N-terminal extension of Arg34GLP-197-37) were ligated and transformed in

E. coli strain MT172 and plasmid DNA was sequenced to verify the correct N-terminally extended Arg34GLP-197-37). Plasmid DNA was then transformed into yeast strain ME1719 and yeast transformants were isolated twice on MUPD selective plates. Yeast cells were cultured in MUPD medium for 3 days and culture supernatants were analyzed by HPLC and MALDI-MS (Matrix As sisted Laser Desorption/Ionization Mass Spectrometry).

L131 ANSWER 6 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **2002-657518** [70] WPIX
DNC **C2002-184505**
TI Producing biologically active dis-aggregated protein from protein aggregates involves using a combination of agitation, high **temperature**, stepped depressurization, and/or dialysis under high pressure.
DC B04 D16
IN CARPENTER, J F; RANDOLPH, T W; ST JOHN, R J; WEBB, J N
PA (UYTE-N) UNIV TECHNOLOGY CORP; (COLS) UNIV COLORADO; (CARP-I) CARPENTER J F; (RAND-I) RANDOLPH T W; (STJR-I) ST J R J; (WEBB-I) WEBB J N
CYC 98
PI WO 2002062827 A2 20020815 (200270)* EN 87 C07K001-113 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2004038333 A1 20040226 (200416) C12P021-06 <--
AU 2002253797 A1 20020819 (200427) C07K001-113 <--
EP 1434789 A2 20040707 (200444) EN C07K001-113 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
JP 2004530651 W 20041007 (200466) 145 C07K001-113 <--
ADT WO 2002062827 A2 **WO 2001-US45728 20011031**; US 2004038333 A1 **Cont of WO 2001-US45728 20011031**, US 2003-425371 20030426; AU 2002253797 A1 **AU 2002-253797 20011031**; EP 1434789 A2 **EP 2001-270119 20011031, WO 2001-US45728 20011031**; JP 2004530651 W **WO 2001-US45728 20011031, JP 2002-563179 20011031**
FDT AU 2002253797 A1 Based on WO 2002062827; EP 1434789 A2 Based on WO 2002062827; JP 2004530651 W Based on WO 2002062827
PRAI **US 2000-244808P 20001031**; US 2003-425371 20030426
IC ICM **C07K001-113**; **C12P021-06**
ICS C07K014-61; C12N007-04
AB WO 200262827 A UPAB: 20021031
NOVELTY - Producing biologically active dis-aggregate protein from protein aggregates or refolding denatured protein involves using a combination of agitation, high **temperature**, stepped depressurization, and/or dialysis under high pressure such that the proteins refolds and the biological activity is retained.

DETAILED DESCRIPTION - Producing biologically active dis-aggregated protein from protein aggregates or refolding denatured protein involves (M1-M5):

(1) M1 comprises:

(a) providing a protein aggregate (I) or denatured protein composition (II);

(b) mixing (I) or (II) with a reducing agent in amount sufficient to reduce disulfide bonds in it;

(c) subjecting the mixture of step (ii) to increased pressure, as compared to ambient pressure, whereby (I) dissolves;

(d) dialyzing the mixture under pressure, whereby the reducing agent is removed and disulfide bonds reform; and

(e) removing the dissolved protein or (II) from increased pressure;

(2) M2 comprises:

(a) providing (I) or (II);
(b) subjecting (I) or (II) to increased pressure, as compared to ambient pressure, and agitation whereby (I) dissolves; and
(c) removing the dissolved protein or (II) from increased pressure;
(3) M3 comprises:
(a) providing (I) or (II);
(b) subjecting (I) or (II) to increased pressure, as compared to ambient pressure, and high **temperature** of about 30 **deg**. C to 125 **deg.** C whereby (I) dissolves; and
(c) removing the dissolved protein or (II) from increased pressure and high **temperature**;
(4) M4 comprises:
(a) providing (I) or (II);
(b) mixing (I) or (II) with a reducing agent in amount sufficient to reduce disulfide bonds in it;
(c) subjecting the mixture of step (b) to increased pressure, as compared to ambient pressure, high **temperature** of about 30 **deg.** C to 125 **deg.** C, and agitation whereby (I) dissolves;
(d) removing or neutralizing the reducing agent, whereby the disulfide bonds reform; and
(e) removing the dissolved protein or (II) from increased pressure and high **temperature**; or
(5) M5 comprises:
(a) providing (I) or (II);
(b) subjecting (I) or (II) to a first increased pressure, as compared to ambient pressure, whereby (I) dissolves;
(c) subjecting the dissolved protein or (II) to a second pressure that is less than the first increased pressure, but still increased pressure as compared to ambient pressure, and
(d) removing the dissolved protein or (II) from second increased pressure, whereby the protein refolds such that biological activity is retained.

Producing biologically active dis-aggregated protein from protein aggregates optionally involves:
(i) providing (I);
(ii) subjecting the mixture of step (i) to increased pressure, as compared to ambient pressure, high temperature of about 30-125 deg. C and agitation, whereby (I) dissolves;
(iii) altering the pH of the mixture of step (i) by dialysis; and
(iv) removing the dissolved protein from increased pressure and high temperature, whereby the protein refolds such that biological activity is retained.

INDEPENDENT CLAIMS are also included for:
(1) rendering (I) susceptible to dissolution by chaotropes, detergents and/or increased temperature comprising subjecting (I) to high pressure in combination with one or more of chaotropes, detergents and/or increased temperature;
(2) screening a protein composition for refolding conditions comprises:
(i) providing a protein composition in physically distinct replicate samples;
(ii) subjecting the replicate samples to different conditions comprising high pressure and varying temperature, buffers of varying pH, buffers of varying salt concentration, varying protein concentration, varying reducing agent concentration, varying stabilizing agents, varying chaotropic agents, varying detergents, varying surfactants; and
(iii) removing the replicate samples from high pressure; and
(iv) assessing protein refolding;
(3) inactivating (M6) virus in a sample containing a desired protein comprise:
(i) providing a sample containing the desired protein, the protein being in a native or non-native state;

(ii) treating the sample to reduce or eliminate infectious virus particles in it; and

(iii) subjecting the sample to a high pressure protein refolding procedure; and

(4) increasing the shelf-life of a protein sample involves removing soluble protein aggregates by applying high pressure, followed by depressurization.

USE - For producing a biologically active dis-aggregated protein from protein aggregates or refolding a denatured protein, where the protein aggregate comprises inclusion bodies, soluble and insoluble precipitates, soluble non-native oligomers, gel, fibrils, films, filaments, protofibrils, amyloid deposits, plaques, or dispersed non-native intracellular oligomers.

(M5) Is preferably useful for producing biologically active dis-aggregated protein from protein aggregate comprising homo-multimeric or hetero-multimeric protein multimers. The multimer may be a dimer, trimer, tetramer, pentamer, hexamer, heptamer, octamer or nonamer. Preferably the multimers are any one of interferon- gamma , hemoglobin, lactic acid dehydrogenase, antibodies or antibody fragments.

(M6) is useful for inactivating virus in sample (e.g., plasma, blood, plasma-derived protein products, a protein product derived from cultured human cells, serum, or serum-containing cell culture medium) that contains or is suspected of containing human immunodeficiency virus (HIV)-1, HIV-2, hepatitis A virus, hepatitis B virus, hepatitis C virus, parvovirus, herpes simplex virus I and II, Epstein-Barr virus, HHV6 or cytomegalovirus (all claimed).

ADVANTAGE - Agitation of protein at various stages, in particular while the protein is under pressure, speeds and improves the dis-aggregation and refolding process. Increasing the temperature during various incubations, including while the protein is undergoing dis-aggregation and refolding, also speeds the process and improve the yield, particularly in the absence of a chaotrope. Removing or reducing the aggregates would reduce the risk of loss of much greater amounts of protein during subsequent processing step due to precipitation.

Dwg.0/15

FS CPI

FA AB; DCN

MC CPI: **B04-C01**; B04-F11; **B04-N04**; B11-B; B11-C08D; B12-K04E; D05-C11; D05-H06; D05-H09; **D05-H13**

TECH UPTX: 20021031

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: (M1) Further involves the step of agitating (I) and/or dissolved protein to enhance dissociation and/or refolding; and subjecting (I) prior to refolding, to a **temperature** of about 30-125degreesC. The steps (ii)-(v) are performed in about 3-12 (preferably 6) hours. The method does not include use of chaotropic agent. Optionally, steps (ii)-(v) are performed in the presence of a chaotropic agent such as guanidine, guanidine sulfate, guanidine hydrochloride, urea, thiocyanate, sarcosyl, sodium dodecyl sulfate, or sodium octyl sulfate, which is then removed.

(M2) Further involves the step of agitating the dissolved protein to enhance refolding, subjecting (I) prior to refolding, to a **temperature** of 30-80degreesC, mixing (I) with reducing agent to reduce disulfide bonds, and dialyzing the mixture under pressure such that the reducing agent is removed and disulfide bonds reform. The reducing agent is optionally removed by diafiltration or ultrafiltration, or by addition of an oxidizing agent. The steps (ii) and (iii) are performed in about 3-12 (preferably 6) hours. The method does not include use of chaotropic agent. Optionally, steps (ii) and (iii) are performed in the presence of a chaotropic agent which is then removed.

(M3) Further involves the step of agitating (I) and/or dissolved protein to enhance dissolution and/or refolding, mixing (I) with reducing agent, and dialyzing the mixture under pressure. The method does not include use of chaotropic agent. Optionally, steps (ii) and (iii) are performed in the

presence of a chaotropic agent which is then removed.
(M4) Further involves dialyzing a mixture under pressure to remove reducing agent, or removing reducing agent by diafiltration or ultrafiltration, or addition of oxidizing agent. The steps (ii) and (iii) are performed in about 1-12 (preferably 6) hours. The method does not include use of chaotropic agent. Optionally, steps (ii) and (iii) are performed in the presence of a chaotropic agent which is then removed. The reducing agent is dithiothreitol, glutathione, dithioerythritol, or beta-mercaptoethanol. The increased pressure comprises about 500-10000 atmospheres.
In (M5), (I) is subjected to a first increased pressure of about 200-1000 MPa, and then subjecting the dissolved protein to second increased pressure of 100 MPa. The method further involves subjecting the protein to high **temperature** of 30-125degreesC, mixing (I), prior to increased pressure, with reducing agent, dialyzing mixture under reduced pressure, to remove reducing agent; or removing reducing agent by diafiltration or ultrafiltration, or addition of oxidizing agent. The (I) is subjected to pressure under high concentration e.g., 5-20 (preferably 10) mg/ml, and diluting (I) to 1 mg/ml under high pressure. The steps (ii)-(iv) are performed in about 3-12 (preferably 6) hours. The method does not include use of chaotropic agent. Optionally, steps (ii)-(iv) are performed in the presence of a chaotropic agent which is then removed.
In (M6), the high pressure protein refolding procedure further comprises one or more of a treatment such as high **temperature**, chaotropic agent, solubilizing agent, reducing agent, agitation or stepped depressurization.

ABEX UPTX: 20021031

EXAMPLE - **Thermally**- and guanidine hydrochloride-induced aggregates of recombinant human interferon gamma (rhIFN-gamma) in buffer at protein concentrations of 1, 10 and 20 mg/mL were pressurized to 250 MPa for five hours. The pressure was then lowered to 100 MPa for one and one-half hours, then again lowered to 0.1 MPa.
Analysis of the pressure treated aggregates was made both immediately following and two weeks after pressure treatment to assess the effectiveness of the pressure treatment on acquisition of native-like characteristics from aggregates and the stability of the pressure-treated aggregates against re-aggregation, respectively. Transmission electron microscopy (TEM), gas-phase electrophoretic mobility mass analysis (GEMMA) and high performance liquid chromatography (HPLC) were employed to physically characterize the pressure-treated aggregates and second derivative UV and Fourier transform infra-red (FTIR) spectroscopies were used to structurally characterize the pressure-treated aggregates.
Upon depressurization, all **thermally**- and guanidine hydrochloride-induced aggregate samples were optically clear with no particulates visible to the eye. Additionally, the 10 and 20 mg/mL **thermally**-induced aggregate samples, which were gelatinous solids prior to pressure treatment, were liquids with viscosities indistinguishable from the native liquid controls. TEM was performed on the liquid control and on the 1 and 20 mg/mL (pressurized and control) samples for both types of aggregates at a total protein concentration of 1 mg/mL (20 mg/mL samples were diluted immediately after pressure treatment. In both pressure-treated samples and the liquid control, amorphous and fibrous structures were observed, with amorphous material more prevalent than fibrous. The observed structures and frequency of amorphous material relative to fibrous material in both pressure-treated aggregates and the liquid control were consistent.
Additionally, there was no observed difference between the samples that were pressure-treated at 1 or 20 mg/mL for both the **thermal** and guanidine hydrochloride-induced aggregates the fibrous network observed in the **thermally**-induced aggregate samples prior to pressure treatment was destroyed and a large proportion of the pressure-treated **thermally** induced aggregate was amorphous. As well, the fibrous material that was observed in the pressure-treated guanidine

hydrochloride-induced sample was not found in the guanidine hydrochloride-induced aggregate controls. Following the pressure-treatment, UV and FTIR absorbancy spectra were collected and second derivative UV and FTIR spectra calculated for pressurized and control samples. The 10 and 20 mg/mL samples were diluted immediately after depressurization such that all UV analysis was conducted at 1 mg/mL rhIFN-gamma. Spectra were recorded at 0.1 MPa after the pressure-treatment protocol.

The extent of recovery of the native second derivative UV spectrum was aggregated-form independent. But the **degree** of recovery of the native second derivative UV spectrum was concentration dependent, with greater recovery of the native spectrum at lower protein concentrations. At 1 mg/mL, the pressure-treated aggregates recovered nearly identical second derivative UV spectra as the native rhIFN-gamma liquid control. The recovery of native secondary structure, measured qualitatively by FTIR, was aggregate-form independent, as the second derivative FTIR spectra at 10 and 20 mg/mL were the same for both aggregate forms, respectively. However, the recovery of native-like secondary structure was dependent on the protein concentration during pressure treatment. There was substantial reduction in the intermolecular beta-sheet bands near 1620 and 1695 cm-1 with pressure treatment for both the 10 and 20 mg/mL samples. But, the reduction of these intermolecular beta-sheet bands to levels observed in the native spectrum was nearly complete for the 10 mg/mL recovered all of the alpha-helix seen in the native structure. The recoveries of native secondary structure, as measured by area of overlap were 90 and 70% for the 10 and 20 mg/mL pressure-treatments, respectively. Two weeks after the pressure refolding was performed, the samples that had been immediately diluted to 1 mg/mL upon depressurization were removed from storage at 4degreesC and analyzed by UV. The spectrum of the 1 mg/mL pressure-treated aggregate sample was the same as the spectrum taken immediately following the pressure treatment and showed essentially full recovery of native-like characteristics.

However, the spectra of the 10 and 20 mg/mL pressure-treated aggregate samples were changed from the respective spectra taken immediately following pressure treatment. Following storage at 1 mg/mL and 4 **degreesC** for two weeks, the recoveries of native structure, as measured by the height of the extremum near 286 nm, were 100, 97 and 94% for the 1, 10 and 20 mg/mL **thermally**-induced, pressure-treated aggregates, respectively. The recoveries of native structure for the 10 and 20 mg/mL **thermally**-induced, pressure-treated aggregates increased from 89 and 79% measured immediately after pressure treatment, respectively.

L131 ANSWER 7 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **2002-537456** [57] WPIX
DNC **C2002-152408**
TI Producing heterologous non-bacterial polypeptides, by culturing yeast strain having polynucleotide encoding polypeptide, under transcriptional control of yeast citrate synthetase gene promoter and isolating the product.
DC B04 D16
IN ANDERSEN, A S; **DIERS, I**
PA (NOVO) NOVO NORDISK AS; (ANDE-I) ANDERSEN A S; (DIER-I) DIERS I
CYC 98
PI WO 2002044388 A1 20020606 (200257)* EN 25 C12N015-81
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2002023018 A 20020611 (200264) C12N015-81
EP 1339856 A1 20030903 (200365) EN C12N015-81

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

JP 2004514450 W 20040520 (200434) 42 C12N015-09
US 2005019853 A1 20050127 (200509) C12P021-02

ADT WO 2002044388 A1 WO 2001-DK782 20011126; AU 2002023018 A AU 2002-23018 20011126; EP 1339856 A1 EP 2001-998644 20011126, WO 2001-DK782 20011126; JP 2004514450 W WO 2001-DK782 20011126, JP 2002-546736 20011126; US 2005019853 A1 Provisional US 2000-256602P 20001219, US 2001-2826 20011130

FDT AU 2002023018 A Based on WO 2002044388; EP 1339856 A1 Based on WO 2002044388; JP 2004514450 W Based on WO 2002044388

PRAI DK 2000-1800 20001130

IC ICM C12N015-09; C12N015-81; C12P021-02
ICS A61K038-28; C12N001-18; C12N001-19; C12N015-60

ICA C12N009-88

ICI C12N009:88

AB WO 200244388 A UPAB: 20021031

NOVELTY - Making (M) a heterologous, non-bacterial polypeptide or its intermediate in yeast, involves culturing a yeast strain comprising a polynucleotide sequence encoding the desired polypeptide or its intermediate, which is under transcriptional control of yeast citrate synthetase gene, CIT1 promoter, its functional portion or variant, under suitable culture conditions, and isolating the expressed product.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a polynucleotide construct (I) comprising a polynucleotide sequence encoding a non-bacterial polypeptide or its intermediate and a DNA sequence encoding CIT1 yeast promoter, its functional portion or variant;

(2) a yeast expression vector (II) comprising in proper reading frame, a polynucleotide sequence comprising a CIT1 yeast promoter, its functional portion or variant, a polynucleotide sequence encoding a non-bacterial polypeptide or its intermediate, a suitable leader sequence, and a possible transcription terminator sequence; and

(3) yeast cells transformed with (I) or (II).

USE - (M) is useful for making a heterologous, non-bacterial polypeptide (or its intermediate) such as insulin precursor, GLP-1(7-37) or GLP-1(7-37)Arg34 in yeast (claimed).

ADVANTAGE - (M) provides an increased yield of heterologous, non-bacterial polypeptide.

Dwg.0/2

FS CPI

FA AB; DCN

MC CPI: B04-E02F; B04-E08; B04-F0900E; B04-N0400E; D05-H12A; D05-H12E; D05-H14A2; D05-H17A6

TECH UPTX: 20020906

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The CIT1 promoter consists of all or portion of a nucleotide sequence (S) of 722 (bp) base pairs defined in the specification, or from nucleotide positions 10-722, 150-722 or 150-530 of (S). The expressed polypeptide is isolated from the culture medium. The method is a batch process.

Preferred Construct: (I) further comprises a leader sequence for secretion of the expressed polypeptide.

ABEX UPTX: 20020906

EXAMPLE - An expression vector encoding a N-terminal extended insulin precursor (B(1-29)-Asp-Pro-Lys-A(1-21)) under expression control of yeast citrate synthetase gene (CIT1) promoter was constructed. An EcoRI/XbaI fragment containing DNA encoding the fusion product (which comprised a signal peptide followed by a synthetic leader, a LysArg cleavage site for the dibasic processing endopeptidase KEX2, a spacer and processing site (GluGluGly-GluGluProLys) and an insulin precursor B (1-29)-AspProLys-A(1-21)), was ligated to the NcoI/XbaI and the NcoI/EcoRI fragment (containing the CIT1 promoter) from pEA268. The resulting plasmids were propagated in Escherichia coli grown in the presence of ampicillin and isolated using

standard techniques. The plasmid DNA was checked for insert by appropriate restriction nucleases (e.g. EcoRI, NcoI, SalI, XbaI) and was shown by sequence analysis to contain the proper sequence of the CIT1 promoter. The plasmid pEA268 was transformed into Saccharomyces cerevisiae strain MT663. Yeast transformants harboring plasmid pEA268 were selected by glucose utilization as carbon source on YPD (1% yeast extract, 2% peptone, 2% glucose) agar (2%) plates and the resulting strain was named yEA268. The control strain MT742 was MT633 transformed with pMT742. The yield obtained using CIT1 promoter compared to the S.cerevisiae TPI promoter was increased. The CIT1 promoter gave 340% increase in expression compared to control in B(1-29)-AspProLys-A(1-21) with N-terminal extension, and secreted product.

L131 ANSWER 8 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2002-417123 [44] WPIX
DNC C2002-117699
TI Monomerizing human serum albumin e.g. recombination technique-produced by treatment with alkaline solution and thiol compound to disrupt intra- and intermolecular misholding, used in surgery, hemorrhagic shock and burns.
DC B04 D16
IN ADACHI, S; MIYATSU, Y; MIZOKAMI, H; NOUCHI, T; SHIBATA, S; TAJIMA, Y; TANABE, T; USHIO, Y; YOKOTE, H
PA (KAGA) CHEMO-SERO-THERAPEUTIC RES INST
CYC 98
PI WO 2002034785 A1 20020502 (200244)* JA 19 C07K014-765 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
JP 2002128793 A 20020509 (200245) 5 C07K001-14 <--
JP 2002128794 A 20020509 (200245) 6 C07K001-14 <--
AU 2002010934 A 20020506 (200257) C07K014-765 <--
KR 2002065607 A 20020813 (200309) C07K014-765 <--
US 2003027991 A1 20030206 (200313) C07K014-765
CN 1406247 A 20030326 (200344) C07K014-765
EP 1329460 A1 20030723 (200350) EN C07K014-765
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2002034785 A1 **WO 2001-JP9334 20011024**; JP 2002128793 A **JP 2000-324027 20001024**; JP 2002128794 A **JP 2000-324028 20001024**; AU 2002010934 A **AU 2002-10934 20011024**; KR 2002065607 A **KR 2002-708240 20020624**; US 2003027991 A1 **Cont of WO 2001-JP9334 20011024, US 2002-175781 20020621**; CN 1406247 A **CN 2001-805647 20011024**; EP 1329460 A1 **EP 2001-978881 20011024, WO 2001-JP9334 20011024**
FDT AU 2002010934 A Based on WO 2002034785; EP 1329460 A1 Based on WO 2002034785
PRAI **JP 2000-324028 20001024; JP 2000-324027 20001024**
IC ICM **C07K001-14**; C07K014-765
ICS **C07K001-14; C12P021-02**
ICA A61K038-00; A61P017-02; A61P043-00; **C12P021-02**
AB WO 200234785 A UPAB: 20020711
NOVELTY - Monomerizing human serum albumin (HSA) polymers by treating with an alkaline solution, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) monomerizing HSA polymers by treating with an alkaline solution in the presence of a thiol (SH group)-containing compound; and

(2) monomerizing HSA polymers by treating with an alkaline solution while preventing misholding of HSA comprising treatment with the alkaline

solution in the presence of a thiol-containing compound.
ACTIVITY - Hemostatic.
No biological data is given.
MECHANISM OF ACTION - None given.
USE - The purified human serum albumin is for use in surgery, hemorrhagic shock, burns, nephrose syndrome and other conditions due to hypoalbuminemia.
ADVANTAGE - The human serum albumin can be produced in high productivity by using transformant yeast, and the polymers in it that are caused by oxidative polymerization during production or in plasma can be efficiently eliminated to give high purity human serum albumin to afford safe drugs without allergic side-effects due to contaminated materials when administered to humans.
Dwg.0/1

FS CPI
FA AB; DCN
MC CPI: **B04-N02**; B05-A01A; B05-A01B; B05-B02C; B05-C01; B05-C08; B10-A04; B10-A07; B10-B02D; B10-B03B; B10-C02; B10-C04E; B14-N17A; **D05-H13**

TECH UPTX: 20020711
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Methods: Concentration of the thiol-containing compound is 0.1-5 mM, particularly 0.2-15 mM, especially 0.5-5 mM. The thiol compound is a low molecular compound including cysteine, cysteamine, cystamine and methionine. The HSA is particularly a recombinant HSA produced by gene recombination method. The pH of the alkaline solution is 8-11, particularly 8.5-9.5, especially 9. Such treatment with the alkaline solution is for not less than 15 minutes, particularly 2-8 hours, especially 3-4 hours, at 0-65 **degrees** C, or room **temperature**. The alkaline solution can be a solution prepared from an alkaline organic or inorganic compound, e.g. a mixture of 2 or more of ammonia, ammonium salt, basic metal hydroxide, borate, phosphate, acetate, oxalate, citrate and trishydroxylaminomethane, particularly a mixture of ammonia, sodium hydroxide, potassium hydroxide, boric acid, borate and trishydroxylaminomethane.

ABEX UPTX: 20020711
EXAMPLE - An rHSA (recombinant human serum albumin) was produced by a transformant Saccharomyces cerevisiae as described in Japanese Patent Hei 11-509525. After 2-fold dilution of the culture liquor and adjusting pH to 4.5 with aqueous acetic acid, the mixture was applied to a Streamline SP (RTM) column (**60** x 16 cm i.d.) equilibrated with 50 mM sodium chloride-containing 50 mM sodium acetate at pH 4.5, with 0.3 mM sodium chloride-containing 50 mM phosphate buffer at pH 9 for elution. The product (10 ml) was treated with 1 mM cysteine and 5 % potassium tetraborate (15 ml) to a finally concentration of 3 % (at pH 9). After storage for 3 hours at room **temperature**, pure rHSA was obtained and the monomer content was determined by gel filtration high performance liquid chromatography (HPLC) (97 % monomer and 3 % polymers).

L131 ANSWER 9 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2002-154921 [20] WPIX
DNC C2002-048495
TI Purifying troponin I comprises subjecting troponin I to chromatography on anion exchanger after reversibly protecting the free sulfhydryl groups.
DC B04 D16
IN CONN, G; REARDON, B; ZENG, X; ZHANG, C
PA (DIOS-N) DIOSYNTH RTP INC; (CONN-I) CONN G; (REAR-I) REARDON B; (ZENG-I) ZENG X; (ZHAN-I) ZHANG C; (ALKU) AKZO NOBEL NV
CYC 95
PI WO 2002004512 A2 20020117 (200220)* EN 28 C07K014-47 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM EC EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK

LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG
SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU	2001073348	A	20020121 (200234)	C07K014-47	<--
US	2002055145	A1	20020509 (200235)	C12P021-02	<--
US	2002064835	A1	20020530 (200240)	C12P021-04	<--
US	2003105017	A1	20030605 (200339)#	A61K038-17	
US	2003138907	A1	20030724 (200352)	C12P021-02	<--
US	6841658	B2	20050111 (200505)	C07K001-14	<--

ADT WO 2002004512 A2 **WO 2001-US21817 20010710**; AU 2001073348 A **AU 2001-73348 20010710**; US 2002055145 A1 **Provisional US 2000-217069P 20000710, Cont of US 2001-903398 20010710, US 2001-998619 20011130**; US 2002064835 A1 **Provisional US 2000-217069P 20000710, US 2001-903398 20010710**; US 2003105017 A1 **Div ex US 2001-903398 20010710, US 2002-255244 20020926**; US 2003138907 A1 **Provisional US 2000-217069P 20000710, Cont of US 2001-903398 20010710, Cont of US 2001-998619 20011130, US 2002-287118 20021104** ; US 6841658 B2 **Provisional US 2000-217069P 20000710, Cont of US 2001-903398 20010710, US 2001-998619 20011130**

FDT AU 2001073348 A Based on WO 2002004512

PRAI **US 2000-217069P 20000710; US 2001-903398 20010710; US 2001-998619 20011130; US 2002-255244 20020926; US 2002-287118 20021104**

IC ICM A61K038-17; **C07K001-14**; C07K014-47; **C12P021-02**; **C12P021-04**

ICS A61K038-00; C07H021-04; **C07K001-16**; C12N001-21; C12N015-00; **C12P021-06**

AB WO 200204512 A UPAB: 20020402

NOVELTY - Preparing troponin I, comprising protecting free sulfhydryl groups of troponin I under reducing conditions, and troponin I is then purified by subjecting troponin I comprising sulfhydryl protecting groups to chromatography, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for troponin I comprising sulfhydryl protecting groups.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Inhibitor of angiogenesis. No supporting data is given.

USE - The method is useful for purifying troponin I, particularly recombinant troponin I. The highly purified troponin I, preferably in a refolded state is useful for antibody generation, as a control or standard immunoassay reagent, or to inhibit angiogenesis important in treating various cancers.

ADVANTAGE - Protection of sulfhydryl groups during troponin I preparation eliminates the costly need for maintaining non-reducing conditions throughout protein preparation, purification and storage, and need for reducing agents. The sulfhydryl-protected troponin does not form intrachain or interchain disulfide crosslinks. Overall yield of troponin from the multi-step purification was greater than 50% at purity levels of greater than 95%. Deprotection of the sulfhydryl groups yields a highly purified product ready for refolding.

Dwg.0/11

FS CPI

FA AB; DCN

MC CPI: B04-F10A3E; **B04-N0400E**; B05-A01B; B11-B; **D05-H13**; D05-H17A6

TECH UPTX: 20020402

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The recombinant troponin I is expressed in a bacterial expression system, preferably an Escherichia coli expression system. The free sulfhydryl groups are protected by sulfitolyzation which comprises reacting reduced recombinant troponin I with sodium tetrathionate. Troponin I is purified by chromatography under non-reducing conditions and the sulfhydryl groups are

deprotected from the purified troponin I. The chromatographic support is an anion exchange column, optionally followed by hydrophobic interaction chromatography. Troponin I is denatured and the sulfhydryl protecting groups are sulfates.

ABEX UPTX: 20020402

EXAMPLE - Human skeletal troponin I (TnI) expressed in Escherichia coli was isolated from lysed cells in inclusion bodies. 10 g of TnI-containing inclusion bodies were solubilized and protein sulfhydryls were sulfitolyzed using 6 M urea (200 ml), Tris (25 mM), sodium sulfite (10 mg/ml), sodium tetrathionate (5 mg/ml) pH 7.5 at ambient **temperature** for 6 hours in the dark. The solubilized material was filtered over a 0.2 micro membrane prior to subsequent processing. Sulfitolyzed recombinant human TnI was purified by a five step process. Solubilized, sulfitolyzed TnI-containing inclusion bodies (200 ml) were loaded onto a 3 l volume Q-sepharose FF column pre-equilibrated in 6 M urea, 25 mM Tris, 0.1 M NaCl pH 7.5 at 150 ml/min. The purified TnI was collected in the column flowthrough. The recovered TnI was concentrated. This material was loaded onto a 300 ml volume Q-sepharose FF column pre-equilibrated in 6M urea, 25 mM Tris, pH 7.5 at 20 ml/minute. The bound TnI was eluted from the column by a step wash with 6 M urea, 25 mM Tris, 80 mM NaCl pH 7.5. This eluted troponin (500 ml) was loaded onto a **60** ml column of Toyopearl 650 M phenyl HIC resin after addition of ammonium sulfate to a final concentration of 1 M. The column was pre-equilibrated with 6 M urea, 25 mM Tris, 1M ammonium sulfate pH 7.5. The purified troponin was collected as the unbound flowthrough from this column, concentrated 2.5-fold and buffer exchanged for storage by UF/DF. Purified TnI was stored frozen at -70 **degrees** C. Protein purity was determined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and reverse phase chromatography and protein identity was confirmed by peptide mapping with peptide mass and fragmentation analysis. Yield determinations for each step were determined by quantitative reverse phase chromatography. Residual DNA levels, measured by DNA threshold, were less than or equal to 12 pg DNA/mg protein. Endotoxin testing of final product by Limulus Amoebocyte Lysate (LAL) (gel-clot) indicated less than or equal to 3 EU/mg protein.

L131 ANSWER 10 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2001-408655 [43] WPIX
DNC C2001-123779
TI Extractive refolding of scrambled and/or polymerized single-chain polypeptide by refolding disulfide bonds without adding chaotropic agent and isolating polypeptide material with correctly positioned disulfide bonds.
DC B04 D16
IN **DIERS, I**
PA (NOVO) NOVO NORDISK AS; (DIER-I) DIERS I; (NOVO) NN AS
CYC 95
PI WO 2001046453 A1 20010628 (200143)* EN 25 C12P021-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001021514 A 20010703 (200164) C12P021-00 <--
US 2002086973 A1 20020704 (200247) C07K014-00 <--
EP 1242610 A1 20020925 (200271) EN C12P021-00 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 6590072 B2 20030708 (200353) A61K038-28
JP 2003530316 W 20031014 (200368) 35 C07K014-62
ADT WO 2001046453 A1 **WO 2000-DK713 20001220**; AU 2001021514 A **AU 2001-21514 20001220**; US 2002086973 A1 **Provisional US**

2000-174658P 20000106, Cont of WO 2000-DK713 20001220, US 2001-767986 20010123; EP 1242610 A1 **EP 2000-984917 20001220, WO 2000-DK713 20001220**; US 6590072 B2 **Provisional US 2000-174658P 20000106, Cont of WO 2000-DK713 20001220, US 2001-767986 20010123**; JP 2003530316 W **WO 2000-DK713 20001220, JP 2001-546949 20001220**

FDT AU 2001021514 A Based on WO 2001046453; EP 1242610 A1 Based on WO 2001046453; JP 2003530316 W Based on WO 2001046453

PRAI **US 2000-174658P 20000106; DK 1999-1845 19991222**

IC ICM A61K038-28; C07K014-00; C07K014-62; **C12P021-00**
ICS **C07K001-00; C07K001-14; C12P021-02; C12P021-06**

AB WO 200146453 A UPAB: 20010801
NOVELTY - Extractive (M1) refolding of scrambled and/or polymerized single-chain polypeptides (I) contained in microbial culture broth (CB) involves adjusting pH of CB to 10-11, adding catalyst for refolding of disulfide bonds without adding chaotropic agent, adjusting pH, centrifuging CB to separate ells, subjecting supernatant to oxidation, and isolating (I) with correctly positioned disulfide bonds by purifying.

USE - (M1) is useful for extractive refolding of scrambled and/or polymerized insulin precursor or insulin precursor analogue, which involves adjusting pH of CB approximately 10-11, adding a catalyst for refolding of disulfide bonds without adding a chaotropic agent, adjusting pH if necessary, centrifugation of the CB to separate cells and cell debris, subjecting the supernatant to oxidation, isolating the single-chain insulin precursor or insulin precursor analogue with correctly positioned disulfide bonds by suitable purification steps, and converting the insulin precursor or insulin precursor analogue into human insulin or a human insulin analogue by suitable enzymatic conversion steps (claimed).

ADVANTAGE - The method may be carried out in a scale from 10 m3 to 1000 m3. The method is simple and the polypeptides or proteins obtain their native conformation directly from the microbial fermentation broth.
Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: **B04-C01; B04-N04**; B11-B; B11-C09; D05-C11; **D05-H13**; D05-H17

TECH UPTX: 20010801
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In first step of (M1), the pH is adjusted by addition of diluted alkali hydroxide and preferably, the CB is diluted from 2% to 500%. The catalyst employed for refolding of disulfide bonds is a thiol compound such as cysteine, mercaptoethanol, glutathione, and dithiothreitol or their mixture (preferably cysteine, HCl). The thiol compound is added in a concentration of 0.2-100 mM (most preferably 2-5 mM). The first step of (M1) is carried out at a **temperature** of 4-35degreesC (more preferably 15-25degreesC) for 20 minutes (preferably 10 minutes). The pH of the third step of (M1) is adjusted to 8.5-10.2 (preferably 9.7). The supernatant in the fifth step of (M1) is subjected to aeration. The method is completed in less than about 120 minutes. The method is preferably carried out for extractive refolding of human insulin precursor or precursor analogue which has ASP at position B28, or Lys at position B28 and Pro in position B29, or Gly in position A21. The insulin precursor or precursor analogue comprise a peptide bridge of 15 residues in length linking the amino acid residue in position B29 in the B chain to the amino acid residue in position A1 in the A chain. Preferably, the peptide bridge is 5 (preferably 3) amino acid residues in length. (M1) involves adjusting pH of the CB to approximately 10-11 by addition of diluted alkali hydroxide (0.1-1 M sodium hydroxide); adding a thiol compound (solid or liquid cysteine, HCl) to the CB to make 1-20 mM; after short period, e.g., 5 minutes, adjusting pH to 7.0-11 if necessary; centrifugation of the CB to

separate cell and cell debris, stirring the supernatant under aeration for 60 to 180 minutes, and isolating single-chain polypeptide material with correctly positioned disulfide bonds by suitable purification steps. Alternately, (M1) involves adjusting pH of CB to approximately 10-11, dilution of the CB to 2-500%; adding a catalyst for refolding of disulfide bonds without adding a chaotropic agent, adjusting pH if necessary, centrifugation of the CB to separate cells and cell debris, subjecting the supernatant to oxidation, and isolating single chain polypeptide material with correctly positioned disulfide bonds by suitable purification steps.

ABEX UPTX: 20010801

EXAMPLE - Saccharomyces cerevisiae strain MT663 was used as host to produce single chain mini-proinsulins. The DNA encoding the mini-proinsulins was synthesized by overlap extension polymerase reactions and cloned into the expression cassette of the vector. The plasmid DNA was transformed into MT663, and transformants selected on YPD plates. The MT663 transformant designed to produce B(1-29)-A(1-21), B28Asp was designated YJB155. A culture broth was prepared by continuous culture of YJB155 on a medium consisting of essential salts and vitamins and yeast extract and glucose as carbon source and ammonia as nitrogen source at pH 5.5 30degreesC. The overflowing broth was collected and stored before extraction. Before extraction, the sample was homogenized by fast stirring. 100 ml of broth was sampled and the **temperature** was slowly adjusted to room **temperature**, 22degreesC. 3 ml of 4 M NaOH diluted with water to a final volume of 50 ml was quickly mixed with the broth at a high stirring rate to reach pH 10.5. Then 0.3 g of cysteine, HCl was added and after 1-2 minutes the cysteine was brought in solution and pH adjusted from 10.8 to 10.5 by addition of 0.44 ml 4 M HCl. The stirrer speed was reduced ad kept constant for another 10 minutes. pH was lowered to 9.7 by addition of 0.53 ml 4 N HCl and the culture centrifuged. The supernatant was removed and stirred as before and no further pH adjustment was necessary. The air oxidation was completed 51 minutes after the beginning of the refolding experiment. Samples were taken at 0, before acidification to pH 9.7 at 11.5 minutes, after centrifugation at the end and all immediately acidified to pH 3 with HCl and run on HPLC to quantify the yield of insulin precursor. The yield of insulin precursor (yield mg/l) at a pH of 9.7 and after 51 minutes was 81.4.

L131 ANSWER 11 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2001-123104 [13] WPIX
DNC C2001-035775
TI Stabilizing proteins in solution, useful particularly during processing of heterologous recombinant proteins, by addition of cysteine.
DC B04 D16
IN KELLER, R; RUBROEDER, F; RUBRODER, F
PA (AVET) AVENTIS PHARMA DEUT GMBH
CYC 94
PI WO 2001002435 A1 20010111 (200113)* GE 21 C07K014-62 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
DE 19930676 A1 20010118 (200113) C07K014-62 <--
AU 2000058164 A 20010122 (200125) C07K014-62 <--
US 6339061 B1 20020115 (200208) A61K038-28 <--
NO 2001006071 A 20011212 (200225) C07K000-00 <--
EP 1196447 A1 20020417 (200233) GE C07K014-62 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002058623 A1 20020516 (200237) A61K038-28 <--
BR 2000012150 A 20020521 (200238) C07K014-62 <--

CN 1357008	A	20020703	(200265)		C07K014-62	<--
KR 2002026515	A	20020410	(200267)		C07K014-62	<--
ZA 2001010507	A	20020925	(200275)	24	C07K000-00	<--
HU 2002002264	A2	20021028	(200277)		C07K014-62	<--
JP 2003504313	W	20030204	(200320)	16	C07K001-14	<--
MX 2001012836	A1	20020801	(200367)		C07K001-00	<--
AU 768443	B	20031211	(200404)		C07K014-62	
NZ 516372	A	20040326	(200425)		C07K014-62	
US 6734164	B2	20040511	(200431)		A61K038-28	
US 2004230038	A1	20041118	(200477)		C07K014-195	

ADT WO 2001002435 A1 **WO 2000-EP5666 20000620**; DE 19930676 A1 **DE 1999-1030676 19990702**; AU 2000058164 A **AU 2000-58164 20000620** ; US 6339061 B1 **US 2000-608297 20000630**; NO 2001006071 A **WO 2000-EP5666 20000620, NO 2001-6071 20011212**; EP 1196447 A1 **EP 2000-943838 20000620, WO 2000-EP5666 20000620**; US 2002058623 A1 **Cont of US 2000-608297 20000630, US 2001-991964 20011126**; BR 2000012150 A **BR 2000-12150 20000620** , **WO 2000-EP5666 20000620**; CN 1357008 A **CN 2000-809177 20000620**; KR 2002026515 A **KR 2002-700032 20020102**; ZA 2001010507 A **ZA 2001-10507 20011221**; HU 2002002264 A2 **WO 2000-EP5666 20000620, HU 2002-2264 20000620**; JP 2003504313 W **WO 2000-EP5666 20000620, JP 2001-508222 20000620**; MX 2001012836 A1 **WO 2000-EP5666 20000620, MX 2001-12836 20011213**; AU 768443 B **AU 2000-58164 20000620**; NZ 516372 A **NZ 2000-516372 20000620, WO 2000-EP5666 20000620**; US 6734164 B2 **Cont of US 2000-608297 20000630, US 2001-991964 20011126**; US 2004230038 A1 **Cont of US 2000-608297 20000630, Cont of US 2001-991964 20011126**, US 2004-796160 20040310

FDT AU 2000058164 A Based on WO 2001002435; EP 1196447 A1 Based on WO 2001002435; BR 2000012150 A Based on WO 2001002435; HU 2002002264 A2 Based on WO 2001002435; JP 2003504313 W Based on WO 2001002435; MX 2001012836 A1 Based on WO 2001002435; AU 768443 B Previous Publ. AU 2000058164, Based on WO 2001002435; NZ 516372 A Based on WO 2001002435; US 6734164 B2 Cont of US 6339061; US 2004230038 A1 Cont of US 6339061, Cont of US 6734164

PRAI **DE 1999-19930676 19990702**

IC ICM A61K038-28; C07K000-00; **C07K001-00**; **C07K001-14**; C07K014-195; C07K014-62

ICS A61K038-00; C07K014-245; C07K014-395; C07K014-435; C07K014-82; C12N001-21; C12N015-63; **C12P021-02**

ICI **C12P021-02**; **C12P021-02**; **C12P021-02**; **C12P021-02**; C12R001:19; C12R001:84; C12R001:865; C12R001:91

AB WO 200102435 A UPAB: 20010307

NOVELTY - Storing a protein (I) in aqueous solvent in which decomposition of the concentration of active (I) is delayed by addition of cysteine, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for preparation of heterologous (I), or its precursor, in which (I) is stabilized by the new method.

USE - For stabilizing recombinant heterologous proteins, particularly (pro)insulin, between the various stages of the production process.

ADVANTAGE - Cysteine reduces the loss of active (I) that occurs during storage in a complex mixture. Solutions of (I) can now be stored for many weeks with only a small loss of activity.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: **B04-J03A**; **B04-N04**; **B04-N0400E**; **D05-H13**; D05-H17

TECH UPTX: 20010307

TECHNOLOGY FOCUS - BIOLOGY - Preferred Material: (I) is a heterologous protein produced in a microorganism, particularly a bacterium, especially Escherichia coli, or a yeast, especially Saccharomyces cerevisiae or Pichia pastoris, or insect cells. It is produced by transformation with a

conventional expression vector and is present in the solvent in dissolved or suspended form. (I) is insulin, its derivative and/or precursor. Preferred process: The concentration of cysteine in the aqueous solution is 100-500, especially 170, mM and storage is at 0-50, preferably 5 **degrees** C. A heterologous (I), or its precursor, is expressed in a transformed cell, then optionally the cell is lysed, or (I) is isolated from the culture medium. It is stored by the novel method, optionally with subsequent renaturing, cleavage of the leader sequence and any other sequences present only in the precursor, and finally purified for isolation of (I).

ABEX UPTX: 20010307

EXAMPLE - A fusion protein of human insulin was produced in Escherichia coli as described in EP 906968. The protein suspension (2500 kg; one fermentation batch) was stirred for 20 minutes with 75 kg cysteine hydrochloride monohydrate (the pH fell from 7 to 2.5), to provide a concentration of 170 mM. Stirring was continued for **60** minutes, then the solution was stored, without stirring, at 5 **degrees** C. Periodically samples were taken and the fusion protein converted to prepro-insulin (A) by reductive folding, and the concentration of (A) determined by high performance liquid chromatography. For samples containing cysteine, the level of (A) was 825-850 mg/l for samples taken between 1 day and 8 weeks of storage, but for those without cysteine, the concentration of (A) fell steadily from 879 mg/l (1 day) to 625 mg/l (8 weeks).

L131 ANSWER 12 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2000-611358 [58] WPIX
DNC C2000-182869
TI Protein crystallization involves adding a salt to aqueous solution of protein to form protein-salt solution, allowing formation of crystal at specific **temperature**, and then introducing a **temperature** shift.
DC B04 D16
IN HENG, M H
PA (GEMV) GENENCOR INT INC; (HENG-I) HENG M H
CYC 88
PI WO 2000052150 A1 20000908 (200058)* EN 14 C12N009-54 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AL AM AT AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 2000033938 A 20000921 (200065) <--
EP 1159410 A1 20011205 (200203) EN C12N009-54 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6403350 B1 20020611 (200244) C12N009-00 <--
CN 1342198 A 20020327 (200247) C12N009-54 <--
JP 2002537804 W 20021112 (200275) 16 C12N009-00 <--
US 2002177206 A1 20021128 (200281) C12P021-06 <--
US 6593118 B2 20030715 (200348) C12N009-100
MX 2001008715 A1 20020801 (200367) C07K001-30 <--
NZ 513163 A 20040227 (200418) C12N009-54
ADT WO 2000052150 A1 **WO 2000-US5564 20000303**; AU 2000033938 A **AU 2000-33938 20000303**; EP 1159410 A1 **EP 2000-912166 20000303, WO 2000-US5564 20000303**; US 6403350 B1 **Provisional US 1999-123147P 19990305, US 2000-518786 20000303**; CN 1342198 A **CN 2000-804627 20000303**; JP 2002537804 W **JP 2000-602762 20000303, WO 2000-US5564 20000303**; US 2002177206 A1 **Provisional US 1999-123147P 19990305, Div ex US 2000-518786 20000303, US 2001-53199 20011102**; US 6593118 B2 **Provisional US 1999-123147P**

19990305, Div ex US 2000-518786 20000303, US 2001-53199 20011102; MX 2001008715 A1 **WO 2000-US5564 20000303 , MX 2001-8715 20010828**; NZ 513163 A **NZ 2000-513163 20000303, WO 2000-US5564 20000303**

FDT AU 2000033938 A Based on WO 2000052150; EP 1159410 A1 Based on WO 2000052150; JP 2002537804 W Based on WO 2000052150; US 2002177206 A1 Div ex US 6403350; US 6593118 B2 Div ex US 6403350; MX 2001008715 A1 Based on WO 2000052150; NZ 513163 A Based on WO 2000052150

PRAI **US 1999-123147P 19990305; US 2000-518786 20000303; US 2001-53199 20011102**

IC ICM **C07K001-30**; C12N009-00; C12N009-100; C12N009-54; **C12P021-06**

ICS C12N009-02; C12N009-04; C12N009-10; C12N009-16; C12N009-26; C30B007-00

AB WO 200052150 A UPAB: 20001114

NOVELTY - Protein crystallization involves preparing an aqueous solution of protein, adding a salt to form protein/salt solution, placing the solution at 4-20 **deg.** C, allowing the formation of crystal nuclei and increasing **temperature** of the solution to 22-**60 deg.** C to allow faster crystallization.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an enzyme crystal produced by the above method.

USE - The method is useful for rapid crystallization of proteins, in particular enzymes, with desired morphology without altering its activity.

ADVANTAGE - The method is inexpensive, efficient for large scale production, and allows rapid production of crystals with a desirable morphology, which represents large savings and is of great importance to industry.

Dwg.0/4

FS CPI

FA AB; DCN

MC CPI: B04-L03A; B04-L04; B04-L05; B04-L07; **B04-N04**; B11-B; D05-C03C; D05-C03D; D05-C03F; **D05-H13**

TECH UPTX: 20001114

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: Protein crystals with a desired morphology are recovered from the solution. The protein is preferably an enzyme such as protease, amylase, lipase, cellulase, oxidase, transferase, dehydratase, reductase, hemicellulase, isomerase or mixtures of these, and the recovered enzyme has at least 90% of its original activity remaining. The aqueous solution of protein is derived from fermentation broth produced by fermentation of a selected microorganism. Cellular debris present in the fermentation broth is removed to produce a cell free filtrate. The aqueous solution is concentrated using an ultrafilter prior to crystallization. The crystallization process results in production of crystals having a desired morphology such as square, rectangle or hexagonal. At least a portion of crystals are square plates. The aqueous solution is maintained at 4-20 **degrees** Centigrade for 5 hours and at 22-**60 degrees** Centigrade for at for 20 hours.

ABEX UPTX: 20001114

EXAMPLE - An aqueous solution comprising an ultra-filtrate concentrate of a fermentation broth of a mutant protease derived from Bacillus subtilis fermentation was prepared. Ultra-filtration was carried out with a polysulfone membrane having a 10 kD molecular weight cut off in a spiral ultra-filtration unit. The resultant protease solution was at a concentration of about 52 g/l of active enzyme. The ultra-filtrate concentrate was equilibrated to the desired starting **temperature** . Sodium chloride (5%) was added with gentle mixing. The solution was maintained at 15 **degrees** Centigrade for four hours and then shifted to 22 **degrees** Centigrade with gentle mixing. Crystal habits were observed over time by examining the sample under a microscope. The activity that remained in the supernatant over time was assayed and the percent crystallization was calculated. Low **temperature** at

the beginning brought about the square shape nuclei but once placed at a higher **temperature**, some crystals were grown to a rod shape. The combination of these resulted in some plates and some rods.

L131 ANSWER 13 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2000-505963 [45] WPIX
DNC C2000-151897
TI Producing and chromatographically purifying recombinant albumin from yeast cells for use in the treatment of burns, shock and blood loss.
DC B04 D16
IN BALLANCE, D J; BEREZENKO, S; CAMERON, J; CARTWRIGHT, A J; GRANDGEORGE, M G J; MEAD, D J; MORTON, P H; SLEEP, D; VAN URK, H; VERON, J B; WOODROW, J R
PA (DELZ) DELTA BIOTECHNOLOGY LTD
CYC 91
PI WO 2000044772 A2 20000803 (200045)* EN 102 C07K014-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000021207 A 20000818 (200057) C07K014-00 <--
EP 1149163 A2 20011031 (200172) EN C12N015-14 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CN 1339065 A 20020306 (200236) C12N015-14 <--
KR 2002008114 A 20020129 (200253) C07K014-765 <--
JP 2002542761 W 20021217 (200312) 92 C12N015-09 <--
AU 763899 B 20030731 (200359) C07K014-00
MX 2001007719 A1 20030601 (200417) C07K014-00
AU 2003248302 A1 20031030 (200431) C07K014-00
CN 1526732 A 20040908 (200478) C07K014-76
ADT WO 2000044772 A2 **WO 2000-GB257 20000131**; AU 2000021207 A **AU 2000-21207 20000131**; EP 1149163 A2 **EP 2000-901252 20000131, WO 2000-GB257 20000131**; CN 1339065 A **CN 2000-803292 20000131**; KR 2002008114 A **KR 2001-709551 20010728**; JP 2002542761 W **JP 2000-596028 20000131, WO 2000-GB257 20000131**; AU 763899 B **AU 2000-21207 20000131**; MX 2001007719 A1 **WO 2000-GB257 20000131, MX 2001-7719 20010730**; AU 2003248302 A1 AU 2003-248302 20030923; CN 1526732 A **Div ex CN 2000-803292 20000131, CN 2004-5015 20000131**
FDT AU 2000021207 A Based on WO 2000044772; EP 1149163 A2 Based on WO 2000044772; JP 2002542761 W Based on WO 2000044772; AU 763899 B Previous Publ. AU 2000021207, Based on WO 2000044772; MX 2001007719 A1 Based on WO 2000044772; AU 2003248302 A1 Div ex AU 763899
PRAI **GB 1999-2000 19990130**
IC ICM C07K014-00; C07K014-76; C07K014-765; C12N015-09; C12N015-14
ICS **C07K001-16**; **C07K001-18**; **C07K001-22**; **C07K001-34**; C12N001-19; C12N015-81; **C12P021-02**; G01N030-00
ICA G01N033-53
ICI **C12P021-02**; **C12P021-02**; **C12P021-02**; C12R001:645; C12R001:84; C12R001:865
AB WO 200044772 A UPAB: 20041216
NOVELTY - Processes ((I)-(III)) for the preparation and purification of highly pure recombinant albumin secreted by a yeast using a series of chromatographic steps, are new. The processes comprise positive and negative mode anion exchange, cation exchange and affinity chromatography. A process (IV) for removing nickel ions from albumin using low pH, is also new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a process (I) for producing recombinant albumin, comprising

culturing a fungal cell expressing a recombinant albumin coding sequence and obtaining the albumin (the cell has genetic modification which causes the cell to have a reduced capacity of mannosylation of the recombinantly-expressed and the culture medium is at least 1000 L and has a pH of 3-6.8 (especially 5));

(2) a process (II) for purifying an albumin solution, comprising subjecting an albumin solution (pH 8.0-9.5, conductivity 1-75 mS.cm-1) to affinity chromatography run in negative mode with respect to the albumin and which utilizes an affinity matrix comprising immobilized dihydroxyboryl groups, therefore obtaining a purified albumin solution;

(3) a process (III) for purifying albumin solution, comprising cation exchange chromatography and/or anion exchange chromatography after which the albumin solution obtained is not purified further before being put into a container; and

(4) a process (IV) for reducing the level of nickel ions in an albumin solution, comprising subjecting an albumin solution to pH 2.5-7.5 (preferably pH 4.0-pH 6.0), and removing the nickel ions.

USE - (I)-(IV) are used for recombinantly producing and purifying albumin which is used for the treatment of patients with severe burns, shock or blood loss. It may also be used for stabilization of other proteins during purification, in cell cultures, in viral production, in vitro fertilization medias and for coating medical devices such as cannulae, catheters and vascular prostheses.

ADVANTAGE - The albumin produced is highly purified and characterized by low levels of colorants (e.g. pigments from the yeast). It is also free from aluminum, lactate, citrate, metals, non-albumin human proteins (e.g. immunoglobulins, pre-kallikrein activator, transferrin, alpha 1-acid glycoprotein, hemoglobin and blood clotting factors), prokaryotic proteins, fragments of albumin, albumin aggregates or polymers, endotoxins, bilirubin, haem, yeast proteins, animal proteins and viruses.

Dwg.0/17

FS CPI

FA AB; DCN

MC CPI: B04-B04D2; B04-B04M; **B04-C01**; B04-E03F; B04-F09C0E; **B04-N0200E**; B11-A; B11-B; B11-C08E1; B11-C09; B12-M07; B14-F02; B14-F11; B14-N17A; B14-S05; D05-C12; D05-H08; D05-H12A; **D05-H13**; D05-H14A2; D05-H17A6; D05-H18

TECH UPTX: 20000918

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Methods: In (I) the modification(s) comprise any suppression, substitution, deletion, addition, disruption and/or mutational insertion. The modifications are stably inherited and/or are non-reverting and/or are non-leaky. The modification are located in a coding region of a gene or in a region involved in the expression of a gene. The gene is a PMT gene, preferably PMT1. The fungal cell is cultured in a medium of at least 5000 L (preferably 7500 L). The cell is cultured at pH 6.2-6.7, preferably, pH 6.3-6.5.

In (II), the pH of the albumin solution is pH 8.0-9.0, preferably pH 8.3-8.6. The solution contains a buffer comprising 10-500 (preferably 25-200, especially 100) mM glycine, 0-500 (preferably 50-150, especially 100) mM NaCl and/or 5-250 (preferably 10-100, especially 50) mM CaCl2. The conductivity of the buffer is 10-50 mS.cm-1, preferably 18-22 mS.cm-1. The solution comprises 70 g.L-1 albumin. The albumins loaded in less than 0.5 column volumes, preferably less than 0.35 column volumes. The matrix comprises immobilized boronic acid, preferably aminophenylboronic acid. The purified solution is subjected to further purification using cation exchange chromatography, to yield a cation exchange purified albumin solution. The solution is then subjected to further purification using anion exchange chromatography, to yield an anion exchange purified albumin solution. A further phase of cation exchange chromatography may also be conducted. The purified albumin solution undergoes buffer exchange, concentration, dilution, dialysis, diafiltration, pH-adjustment, treatment with a reducing agent, decoloration treatment, **heating**

cooling and/or conditioning.
In (III) the cation exchange step is run in negative mode with respect to the albumin. Glycosylated albumin binds to the cation exchange material. The cation exchange step utilizes a matrix comprising immobilized sulfopropyl substituents as cation exchangers. The albumin undergoes cation exchange chromatography at pH 4.5-6.0, preferably pH 5.0-5.6, especially 5.2-5.4. The albumin solution used in the cation exchange chromatography has an albumin concentration of 10-250 g.L-1 (preferably 20-70 g.L-1, especially 50+/-10 g.L-1) and an octanoate ion concentration of 2-15 mM (preferably 5-10 mM, especially 6-9 mM). Prior to cation exchange, the albumin solution undergoes:
(i) pH-adjustment;
(ii) concentration;
(iii) diafiltration; and/or
(iv) conditioning by addition of octanoate and/or other fatty acid.
The anion exchange step utilizes a matrix comprising immobilized dialkylaminoalkyl substituents as anion exchangers. The anion exchange step is run in negative mode with respect to the albumin. The albumin undergoes anion exchange chromatography at pH 4.0-5.2, preferably pH 4.2-4.9, especially 4.5-4.7. The albumin solution also has a conductivity of less than 4.0 mS.cm-1, preferably 1.0 +/- 0.5 mS.cm-1, especially 1.05 +/- 0.1 mS.cm-1. Alternatively, the anion exchange step is run in positive mode with respect to the albumin. In this case, the albumin undergoes anion exchange chromatography at pH 6.0-8.0, preferably pH 6.5-7.5, especially 6.8-7.2. The albumin solution also has a conductivity of 1.0-2.0 mS.cm-1, preferably 1.2 +/- 1.6 mS.cm-1, especially 1.3-1.5 mS.cm-1. The concentration of the albumin solution that undergoes positive mode anion exchange chromatography is 10-100 g.L-1, preferably 25-80 g.L-1, especially 40-**60** g.L-1. The albumin is eluted from the anion exchanger using a buffer (pH 6.0-8.0, preferably pH 6.5-7.5) comprising a compound with a specific affinity for albumin, preferably an acid. the compound may be 35-65 mM of a phosphoric acid salt, preferably sodium phosphate. Prior to anion exchange, the albumin solution undergoes:
(i) buffer exchange;
(ii) concentration;
(iii) dilution;
(iv) dialysis;
(v) diafiltration;
(vi) pH-adjustment;
(vii) treatment with a reducing agent;
(viii) decoloration treatment;
(ix) **heating**;
(x) **cooling**; and/or
(xi) conditioning.
Methods (II) and/or (III) are preceded by:
(i) fermentation;
(ii) primary separation;
(iii) centrate conditioning;
(iv) cation exchange chromatography (using sulfopropyl substituents as cation exchangers);
(v) anion exchange chromatography (using diethylaminoalkyl substituents as anion exchangers); and/or
(vi) affinity chromatography (using an affinity matrix comprising an immobilized albumin-specific dye, preferably a Cibacron Blue (RTM) type of dye).
Methods (II) and (III) may be utilized in conjunction to purify albumin solutions. For example, by subjecting it to:
(A) a cycle of cation exchange chromatography and anion exchange chromatography run in positive and negative modes with respect to albumin (i.e. method (III) as described above);
(B) a phase of affinity chromatography run in a positive mode with respect to albumin (i.e. method (II) as described above);
(C) a phase of affinity chromatography run in a negative mode with respect

to albumin and in positive mode with respect to glycoconjugates (i.e. method (II) as described above); and
(D) a further cycle of cation exchange chromatography and anion exchange chromatography run in positive and negative modes with respect to albumin (i.e. method (III) as described above).
The albumin solution is collected between each stage. The mode of the cation exchange and anion exchange procedures used in (A) and (D) are opposite (e.g. if positive mode anion exchange is used in (A), negative mode anion exchange is used in (D)).
Method (IV) comprises diafiltration or gel permeation chromatography.
The albumin used in (II) to (IV) is recombinant and obtained from a yeast culture medium obtained by culturing yeast transformed with an albumin-encoding nucleotide sequence in a fermentation culture so that the yeast expresses albumin and secretes it into the medium. The yeast is Saccharomyces, especially S. cerevisiae.

ABEX UPTX: 20000918

ADMINISTRATION - The albumin produced is parenterally administered intravenously, subcutaneously or intramuscularly.

EXAMPLE - Albumin was concentrated and purified with respect to yeast proteins (the albumin is rHA (recombinant human albumin) from a yeast fermentation) and other antigens, low molecular weight contaminants and pigmented compounds by cation exchange chromatography. The method used a commercial cation exchange matrix such as SP-Sepharose FF (RTM), which, when used in an axial flow column, had a bed height of 12.5 cm. If a radial flow-type column was used, a suitable bed flow path length was 11.0+/-1.0 cm. A column loading of 40+/-10 g albumin/L of matrix was used. The matrix was equilibrated with a buffer to remove the alkali storage solution (the buffer was strong enough to reduce the pH to approximately pH 6.0). CS01 buffer was used to remove storage solution CS07 from the column. Equilibration was judged to be complete when the pH of the column effluent was pH 6.0. The centrate from a fermentation was prepared, or conditioned, for chromatography on a cation exchange matrix while protecting the rHA from polymerisation and protease activity. 10 M sodium octanoate was sufficient to protect the rHA from **heat** denaturation and 30 seconds at a **temperature** of 80 **degreesC** was adequate to inactivate the proteases in a batch procedure.
The conditioned centrate was then loaded onto the column at a flow rate of 0.07-0.75 bed volumes/minute and then the column was washed with one or more solutions to remove residual contaminants. The column was washed first with eight volumes of 30-70 mM acetate, pH 3.9, 0.6-0.8 mS.cm-1 (CS02). The column was then washed with four volumes of a high salt buffer containing 27 mM sodium acetate, pH 4.0 (CS03) and then ten volumes of CS01. The albumin was eluted with, and collected in an acetateloctanoate buffer (85 mM acetate and 5 mM octanoate, as in CS04). The collection of albumin started when the UV signal rose above 0.6 A254/cm, and collection continued until the UV signal fell below 0.36 A254/cm. The column was then cleaned using 3.0 M NaCl and 2% detergent (CS05) and then 0.1-1.0 M NaOH (CS06), then stored in diluted NaOH (CS07). In this example, the flow rate for the equilibration, loading and wash steps was 0.5 bed volumes per minute.

L131 ANSWER 14 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **2000-271404** [23] WPIX
DNC **C2000-082896**
TI Obtaining substantially pure C-beta protein or fragment and/or mutant for eliciting antibodies which are bactericidal to gram positive bacteria, useful in vaccines.
DC B04 D16
IN BLAKE, M S; LONG-ROWE, K O
PA (BAXT) BAXTER HEALTHCARE SA; (NAVA-N) NORTH AMERICAN VACCINE INC; (BAXT-N) BAXTER HEALTHCARE SA; (BAXT-N) BAXTER BIOTECH TECHNOLOGY SARL

CYC 90
PI WO 2000015760 A1 20000323 (200023)* EN 171 C12N001-06 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ
TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 9960495 A 20000403 (200034) C12N001-06 <--
NO 2001001381 A 20010319 (200134) C12N000-00 <--
EP 1114143 A1 20010711 (200140) EN C12N001-06 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
CZ 2001000951 A3 20011114 (200175) C12N001-06 <--
SK 2001000348 A3 20020205 (200213) C12N001-06 <--
HU 2001003502 A2 20020128 (200222) C12N001-06 <--
JP 2002525041 W 20020813 (200267) 181 C12N015-09 <--
AU 2004201101 A1 20040408 (200456)# C12N001-06
ADT WO 2000015760 A1 **WO 1999-US21643 19990917**; AU 9960495 A **AU 1999-60495 19990917**; NO 2001001381 A **WO 1999-US21643 19990917 , NO 2001-1381 20010319**; EP 1114143 A1 **EP 1999-969108 19990917, WO 1999-US21643 19990917**; CZ 2001000951 A3 **WO 1999-US21643 19990917, CZ 2001-951 19990917**; SK 2001000348 A3 **WO 1999-US21643 19990917, SK 2001-348 19990917**; HU 2001003502 A2 **WO 1999-US21643 19990917, HU 2001-3502 19990917**; JP 2002525041 W **WO 1999-US21643 19990917, JP 2000-570287 19990917**; AU 2004201101 A1 **Div ex AU 1999-60495 19990917**, AU 2004-201101 20040316
FDT AU 9960495 A Based on WO 2000015760; EP 1114143 A1 Based on WO 2000015760; CZ 2001000951 A3 Based on WO 2000015760; SK 2001000348 A3 Based on WO 2000015760; HU 2001003502 A2 Based on WO 2000015760; JP 2002525041 W Based on WO 2000015760
PRAI **US 1999-154017P 19990915; US 1998-100859P 19980917; US 1999-144324P 19990719**; AU 2004-201101 20040316
IC ICM C12N000-00; C12N001-06; C12N015-09
ICS A01N043-04; A61K038-00; A61K039-02; A61K039-09; A61K039-116; A61K039-385; A61K045-00; A61K045-06; A61P031-04; C07H021-02; C07H021-04; **C07K001-00**; **C07K001-14**; **C07K001-18**; **C07K001-22**; C07K014-315; C07K019-00; C12N001-12; C12N001-15; C12N001-19; C12N001-21; C12N005-10; C12N015-00; **C12P021-02**; **C12P021-04**
ICI C12N015-09; C12R001:46
AB WO 200015760 A UPAB: 20000516
NOVELTY - A process for obtaining a substantially pure C beta protein (fragment and/or mutant) is new and comprises:
(a) obtaining the C beta protein in cell extracts;
(b) subjecting the C beta protein to ion-exchange chromatography and collecting the C beta protein-containing fractions;
(c) pooling and diluting the fractions; and
(d) subjecting the fractions to ligand affinity chromatography and collection.
DETAILED DESCRIPTION - A process for obtaining a substantially pure C beta protein (fragment and/or mutant) is new and comprises:
(a) obtaining the C beta protein in cell extracts;
(b) subjecting the C beta protein to ion-exchange chromatography and collecting the C beta protein-containing fractions;
(c) pooling and diluting the C beta protein containing fractions; and
(d) subjecting the diluted C beta protein-containing fractions to ligand affinity chromatography and collecting the fractions; where substantially pure C beta protein or a fragment and/or mutant is obtained.
INDEPENDENT CLAIMS are also included for the following:
(1) an isolated nucleic acid molecule (Ia) coding for a protein

fragment or peptide comprising a proline rich region where at least every third residue is proline and where antibodies raised against the protein fragments or peptides are bactericidal to gram positive bacteria with complement alone;

(2) an isolated nucleic acid molecule (Ib) coding for a protein fragment or peptide having the formula Y-X-Z, the protein fragment or peptide does not bind to the Fc region of human IgA immunoglobulin, with the proviso that the protein is at least one of an N-terminal or C-terminal fragment of a 4200 amino acid sequence (i) (fully defined in the specification), with the proviso that the protein fragment or peptide is not the approximately 38 kD polypeptide secreted by the group B streptococcus strain HG 806 and with the further proviso that at least one of the amino acids 1-164 of the 4200 amino acid sequence , if present in Y is non-wild-type;

(3) a vector (II) comprising (Ia) or (Ib);

(4) a host cell (III) transformed with (II);

(5) a protein or peptide (IV) encoded by (Ia) or (Ib);

(6) a protein fragment or peptide-polysaccharide conjugate (V) comprising (IV); and

(7) a method of inducing an immune response in a mammal comprising administering a vaccine comprising at least (IV) with a pharmaceutically acceptable carrier in an amount sufficient to induce an immune response in a mammal.

X = at least 8 contiguous amino acids between amino acids 827 and 1028 inclusive of a 4200 amino acid sequence (i) (fully defined in the specification);

Y = H, or the N-terminal amino acid of (i) that is bound to X, or an N-terminal fragment and/or mutant; and

Z = H or the C-terminal amino acid sequence of (i) that is bound to X or a C-terminal fragment and/or mutant.

ACTIVITY - Bactericidal.

MECHANISM OF ACTION - Vaccine.

USE - The protein fragments are useful for eliciting antibodies which are bactericidal to gram positive bacteria with complement alone and therefore is useful in a (combination) vaccine together with a pharmaceutically acceptable carrier (and/or optionally at least two protein fragments or peptide-polysaccharide conjugates) (claimed). The vaccine therefore is useful in a method for inducing an immune response in a mammal (claimed).

ADVANTAGE - No advantages stated in the specification.

Dwg.0/23

FS CPI

FA AB; DCN

MC CPI: **B04-C01G**; B04-C02; B04-E02F; B04-E03F; B04-E08; B04-F01; B04-F0100E; B04-G01; **B04-N04**; B11-C08D2; B14-A01B; B14-G01; B14-S11B; D05-C12; D05-H07; D05-H10; D05-H11; D05-H12A; D05-H12E; **D05-H13**; D05-H14; D05-H17

TECH UPTX: 20000516

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Process: The ion-exchange chromatography is performed using an anion exchange medium comprising a triethylaminomethyl group. The ligand-affinity chromatography is performed using a ligand-affinity medium comprising a heparin ligand. The Cbeta protein and/or fragment and/or mutant is subjected to chromatography in a buffer containing about 5% of a zwitterionic detergent. The pooled fractions from the ion exchange chromatography containing the Cbeta protein and/or fragment and/or mutant are diluted approximately three-fold with the buffer containing about 10-20 % of a zwitterionic detergent before the ligand-affinity chromatography. The Cbeta protein or fragment and/or mutant is eluted during the ion-exchange or ligand affinity chromatography medium by applying an eluant comprising a salt gradient. The eluant comprises about 0.5 % of a zwitterionic detergent. The Cbeta protein and/or fragment and/or mutant is obtained from bacterial cells which are transfected with nucleotide sequences encoding the Cbeta

protein or a fragment and/or mutant where the cells overexpress the Cbeta protein or fragment and/or mutant. The Cbeta protein and/or fragment and/or mutant is obtained by:
(a) disrupting the cells;
(b) precipitating non-proteinaceous material from the cells by adding ethanol/CaCl2 to a concentration of about 20% (v/v) ethanol/about 0.1 M CaCl2;
(c) removing the precipitated non-proteinaceous material to give a solution;
(d) precipitating the protein from the solution by adding ethanol to a concentration of about 80% (v/v) and collecting the precipitated protein; and
(e) resuspending the precipitated protein in a buffer solution containing from 1-10% of a zwitterionic detergent.
The Cbeta protein is obtained from bacterial cells which naturally produce the Cbeta protein. The Cbeta protein is also obtained by:
(a) boiling the bacterial cells in a buffer containing from 1-10 % of a zwitterionic detergent to give a solution;
(b) **cooling** the solution in an ice bath;
(c) precipitating non-proteinaceous material from the cells by adding a **cold** solution of ethanol/CaCl2 to give a concentration of about 20 % ethanol/about 0.1 M CaCl2;
(d) removing the precipitated non-proteinaceous material to give a solution;
(e) precipitating protein from the solution by adding ethanol to a concentration of about 80% (v/v) and collecting the precipitated protein; and
(f) resuspending the precipitated protein in a buffer solution containing from 1-10 % of a zwitterionic detergent.
Preferred Molecule: The nucleic acid molecule (I) comprises a continuous repeated amino acid sequence having the formula (A) or (B):
(A) -(P-Y1-Y2-P-Y1-Y2)r-; or
(B) -(Y1-Y2-P-Y1-Y2-P)r-;
Y1 = an acidic or basic residue;
Y2 = neutral amino acid; and
r = 1-5;
or comprises a continuous (repeated) amino acid sequence having the formula (a) or (b):
(a) -(P-D-Y3-P-K-L)r-; or
(b) -(K-L-P-D-Y3-P)r-;
Y3 = Val or Ala;
r = 1-5;
or comprises a continuous (repeated) amino acid sequence comprising the formula (1):
(1) -(S-P-K-Y4-P-E-A-P-Y5-V-P-E)R-;
Y4 = Thr or Ala;
Y5 = H or Arg; and
r = 1-5.
Y does not comprise at least amino acids 1-176 of (i) and Z comprises at least amino acid 901 of (i). X is selected from a group of peptides as follows:
(1) PPKTPDVP;
(2) PDVPKLPD;
(3) KLPDVPKL;
(4) VPKLPDVP;
(5) KLPDAPKL;
(6) APKLPDGL;
(7) ETPDTPKI;
(8) RTVRLALG;
(9) GGGTVRVF;
(10) SPKTPEAPKIPEPPKTPDVP;
(11) PEAPKIPEPPKTPDVPKLPD;
(12) KIPEPPKTPDVPKLPDVPKL;

(13) PPKTPDVPKLPDVPKLPDVP;
(14) PDVPKLPDVPKLDVPKLPD;
(15) KLPDVPKLPDVPKLPDAPKL; AND
(16) PDVPKLPDVPKLPDVPKLPDAPKL.
X represents 8-21 contiguous amino acid residues between amino acids 828 and 1027 inclusive of (i).

ABEX UPTX: 20000516
EXAMPLE - Native Cbeta protein was recovered from the membrane of Streptococcus agalctiae by boiling the bacteria in buffer containing 5% Zwittergent 3, 14 and 25 mM Tris(HCl), pH 7.6-7.8. After boiling, the suspension was **cooled** to 0-10 **degreesC** in an ice bath, then a **cold** (0-4 **degreesC**) solution of ethanol/CaCl2 was added to a final concentration of 20% ethanol/0.1 M CaCl2. The solution was clarified by centrifugation, after which proteins were precipitated from the supernatant with 80% ethanol. Protein was resolubilized in a buffer containing 5% Zwittergent, 25 mM Tris(HCl), 5 mM DTT and PEFABLOC PLUS protease inhibitor, pH 7.6-7.8.

L131 ANSWER 15 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2000-256990 [22] WPIX
DNC C2000-078559
TI Mushroom-derived antibacterial protein against plant pathogenic fungi of rice, with activity and **thermal** stability, obtainable cheaply on large scale, useful in agriculture.
DC C05 D16
IN KUWATA, S; OHTA, S; TAKAKURA, Y
PA (NISB) JAPAN TOBACCO INC; (NORQ) NORIN SUISAN SENTAN GIJUTSU SANGYO ZH; (NORQ) SOC TECHNO-INNOVATION AGRIC FORESTY & FI
CYC 24
PI WO 2000014242 A1 20000316 (200022)* JA 52 C12N015-31 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA CN KR US
JP 2000083675 A 20000328 (200026) 23 C12N015-09 <--
AU 9953009 A 20000327 (200032) C12N015-31 <--
ADT WO 2000014242 A1 **WO 1999-JP4441 19990819**; JP 2000083675 A **JP 1998-270606 19980908**; AU 9953009 A **AU 1999-53009 19990819**
FDT AU 9953009 A Based on WO 2000014242
PRAI **JP 1998-270606 19980908**
IC ICM C12N015-09; C12N015-31
ICS A01N037-12; A01N063-00; A01N063-02; A01N065-00; A61K031-16; **C07K001-14**; **C07K001-18**; **C07K001-30**; C07K014-375; C12N001-19; C12N001-21; C12N005-10; C12Q001-68
ICA **C12P021-02**
ICI C12N015-09; C12R001:645
AB WO 200014242 A UPAB: 20000508
NOVELTY - Cheap-to-make antibacterial protein with activity against at least Pyricularia orizae and Rhizoctonia solani is obtained from a fraction of an aqueous extract of a mushroom precipitated by the ammonium sulfate precipitation method, which has a molecular weight of about 210 kD as determined by the gel filtration method, includes components of about 15 kD and 50 kD in SDS-PAGE, and is stable to **heating** in an aqueous neutral solution at **60 deg.** C for 10 minutes but with loss of antibacterial activity after **heating** in the solution at 80 **deg.** C for 10 minutes.
DETAILED DESCRIPTION - Antibacterial protein with activity against at least Pyricularia orizae and Rhizoctonia solani is obtained from a fraction of an aqueous extract of a mushroom precipitated by the ammonium sulfate precipitation method, which has a molecular weight of about 210 kD as determined by the gel filtration method, includes components of about 15 kD and 50 kD in SDS-PAGE, and is stable to **heating** in an aqueous neutral solution at **60 deg.** C for 10 minutes but with loss of antibacterial activity after **heating** in the

solution at 80 **deg.** C for 10 minutes

INDEPENDENT CLAIMS are also included for:

(1) an antibacterial protein with the desired anti-fungal activity containing a 564 amino-acid sequence (2) (fully defined in the specification), or one based on (2) but with some amino-acids mutated or with not less than 50% homology to the sequence;

(2) a similar antibacterial protein made from a combination of a polypeptide with partial sequences from positions 1-25 of (2), that based on 26-435 of the sequence, that based on 436-564 of the sequence, that based on 1-435 of the sequence, that based on 26-564 of the sequence or/and polypeptides as above but with some amino-acids mutated or/and those with not less than 50% homology to the amino-acid sequence;

(3) a process for producing the antibacterial protein comprising the precipitation of an aqueous mushroom extract with 75% saturated ammonium sulfate with recovery of the precipitated fraction; and ion-exchange chromatography of the fraction with a gradient of 0.35-0.6 M sodium chloride for elution;

(4) a gene encoding the antibacterial protein;

(5) a method for preparing an oligonucleotide obtained from the gene encoding the mushroom-originated antibacterial protein with a 1946 nucleotide sequence (1) (fully defined in the specification) that can satisfy at least 1 of:

(a) each region with a length of 15-30 bases; and

(b) G+C proportion in each region being 40-**60%**, which comprises the preparation of a single-stranded DNA with the above region or similar base sequences or their complementary base sequences, or anther single-stranded DNA with a mixture of base sequences or modified base sequences to encode mutated amino-acids if necessary but without affecting the specific binding activity;

(6) a method for isolating the gene by using 2 of the oligonucleotides as primer pair for nucleic-acid amplification reaction with a mushroom fruiting body cDNA library as template to give a partially amplified gene that encodes the protein, using the amplification product as probed for screening the cDNA library to isolate the full-length cDNA clone;

(7) a recombinant vector containing the gene; and

(8) a transformant obtained by introduction of the recombinant vector.

ACTIVITY - Antibacterial activity.

MECHANISM OF ACTION - Antibacterial agent; anti-fungal.

USE - The protein is for inhibiting the growth of plant pathogenic fungi e.g. Pyricularia orizae and Rhizoctonia solani, useful in treating rice plants, applicable in agriculture as antibacterial (claimed).

ADVANTAGE - Such protein has activity at relatively low concentration, is stable to **heating** to **60 deg** . C for 10 minutes, and can be produced at low cost on large scale.

Dwg.0/8

FS CPI

FA AB; DCN

MC CPI: **C04-C01G**; C04-E02F; C04-E03F; C04-E05; C04-E08; C04-N03A; C11-C08E; C11-C08E5; C14-A01; C14-A04; C14-U02; D05-C12; D05-H12A; D05-H12D1; D05-H12E; **D05-H13**; D05-H14; D05-H17; D05-H18B

TECH UPTX: 20000508

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Protein: The 50 kD component has an N-terminal of a 19 amino-acid sequence (3) (details available), and the 25 kD component has an N-terminal amino-acid sequence of (details given). Such antibacterial protein has not less than **60%**, particularly not less than 70%, especially not less than 80%, more particularly not less than 90%, preferably not less than 95% homology to the amino-acid sequence of (2). Such antibacterial protein is originated from Tricholoma matsutake.

Preferred Gene: The gene has a base sequence (1), or one based on the sequence but with some bases substituted, deleted, inserted and/or added,

or one hybridized with the above base sequence under stringent conditions. Such gene particularly has not less than 50%, particularly not less than 60%, especially not less than 70%, more particularly not less than 80%, more especially not less than 90%, preferably not less than 95%, homology to the bases sequence (1).
Preferred Oligonucleotide: Such oligonucleotide particularly has one of a 23, 23, 20, 21, 20 nucleotide sequences (5) - (9) respectively.
Preferred Vector: The recombinant vector is particularly an expression vector.

ABEX UPTX: 20000508
ADMINISTRATION - The protein can be formulated into granules and solutions.

EXAMPLE - Tricholoma matsutake (10 g) was chopped then frozen with liquid nitrogen for grinding for extraction with 3-fold in amount of 50 mM Hepes buffer, followed by precipitation with ammonium sulfate and purification of the precipitate by ion-exchange chromatography on a MonoQ HR5/5 column, with gradient elution with sodium chloride solution. Complete inhibition of growth of the purified material against Pyricularia orizae was 20 ng/ml. From the protein, cDNA was also isolated for in biotechnological studies.

L131 ANSWER 16 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2000-185076 [17] WPIX
DNC C2000-058187
TI New protein with methanol dehydrogenase promoting activity produced by culturing cell in medium and isolating produced protein.
DC B04 D16
IN YASUEDA, H
PA (AJIN) AJINOMOTO CO INC; (AJIN) AJINOMOTO KK
CYC 29
PI EP 984066 A2 20000308 (200017)* EN 12 C12N015-31 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2000069976 A 20000307 (200023) 10 C12N015-09 <--
CN 1251839 A 20000503 (200036) C07K014-32 <--
BR 9904065 A 20001017 (200056) C12N009-04 <--
US 6280972 B1 20010828 (200151) C12P021-06 <--
EP 984066 B1 20050112 (200505) EN C12N015-31
R: DE FR GB IT
DE 69923127 E 20050217 (200514) C12N015-31
ADT EP 984066 A2 **EP 1999-116831 19990902**; JP 2000069976 A **JP 1998-248297 19980902**; CN 1251839 A **CN 1999-121647 19990902**; BR 9904065 A **BR 1999-4065 19990902**; US 6280972 B1 **US 1999-387800 19990901**; EP 984066 B1 **EP 1999-116831 19990902**; DE 69923127 E **DE 1999-623127 19990902, EP 1999-116831 19990902**
FDT DE 69923127 E Based on EP 984066
PRAI **JP 1998-248297 19980902**
IC ICM C07K014-32; C12N009-04; C12N015-09; C12N015-31; **C12P021-06**
ICS C07H021-04; **C07K001-00**; C12N001-21; C12N015-32; C12N015-53; C12N015-70; C12N015-75; **C12P021-02**; C12Q001-68
AB EP 984066 A UPAB: 20000405
NOVELTY - A protein is new and has an activity to promote methanol dehydrogenase activity.
DETAILED DESCRIPTION - A protein is new and comprises (A) or (B): (A) a protein which comprises a 185 amino acid sequence (fully defined in the specification); or (B) a protein which comprises 185 amino acid sequence and further comprises a substitution, deletion, insertion, addition or inversion of one or more amino acids and has the activity to promote methanol dehydrogenase activity.
INDEPENDENT CLAIMS are also included for the following:
(1) a DNA coding for (A) or (B);

(2) a cell to which a DNA is introduced in such a manner that a protein encoded by the DNA can be expressed; and
(3) a method for producing a protein having an activity to promote methanol dehydrogenase activity which comprises culturing the cell in a medium to produce and accumulates the protein and collecting the protein.
ACTIVITY - None given.
MECHANISM OF ACTION - Promotes methanol dehydrogenase activity.
USE - The protein and DNA is useful for promoting methanol dehydrogenase activity (claimed).
ADVANTAGE - The method enables the efficient production of the factor and therefore can be provided in a large scale and at low cost.
Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: **B04-C01G**; B04-E02F; B04-E03F; B04-E05; B04-F0100E; B04-L03D; **B04-N04**; **B04-N0400E**; D05-C03B; D05-H08; D05-H12A; D05-H12D1; **D05-H13**; D05-H14; D05-H17A3; D05-H17B3
TECH UPTX: 20000405
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred DNA: The DNA comprises:
(a) a DNA which comprises a 555 nucleotide sequence (fully defined in the specification); or
(b) a DNA which is hybridizable with the 555 nucleotide sequence or a probe prepared from the nucleotide sequence under stringent conditions and codes for a protein having an activity to promote methanol dehydrogenase activity.
The stringent condition is a condition in which washing is performed at **60 degreesC** and at a salt concentration of 1 x SSC and 0.1% SDS.
ABEX UPTX: 20000405
EXAMPLE - MDH-BM-1 and MDH-BM-2 DNA primers were used and PCR was carried out. A DNA fragment of a desired size was obtained and the DNA fragment was purified and cloned into a commercially available vector. This was then introduced into Escherichia coli JM109 strain to construct a transformant. MDH activity was measured by estimating the reduction of NAD+ accompanying the oxidation of methanol into formaldehyde through measurement of absorbance for light at 340 nm.

L131 ANSWER 17 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **2000-182222** [16] WPIX
DNC **C2000-056934**
TI Producing peptides of high or low isoelectric point, particularly natriuretic peptides for treating congestive heart failure, by expression as cleavable fusion protein of nearly neutral isoelectric point.
DC B04 D16
IN BUCKLEY, D I; HARTMAN, T E; POLLITT, N S; STATHIS, P A; ZHONG, Z
PA (SCIO-N) SCIOS INC
CYC 87
PI WO 2000003011 A2 20000120 (200016)* EN 39 C12N015-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9948595 A 20000201 (200028) C12N015-00 <--
EP 1095141 A2 20010502 (200125) EN C12N015-12 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6303340 B1 20011016 (200164) C12P021-04 <--
CN 1313896 A 20010919 (200202) C12N015-12 <--
JP 2002520018 W 20020709 (200259) 44 C12N015-09 <--
CN 1521261 A 20040818 (200477) C12N015-62
ADT WO 2000003011 A2 **WO 1999-US15147 19990708**; AU 9948595 A **AU**

1999-48595 19990708; EP 1095141 A2 **EP 1999-932242 19990708**, **WO 1999-US15147 19990708**; US 6303340 B1 **Provisional US 1998-92423P 19980710, US 1999-349644 19990708**; CN 1313896 A **CN 1999-809946 19990708**; JP 2002520018 W **WO 1999-US15147 19990708, JP 2000-559232 19990708**; CN 1521261 A **Div ex CN 1999-809946 19990708, CN 2003-1123344 19990708**

FDT AU 9948595 A Based on WO 2000003011; EP 1095141 A2 Based on WO 2000003011; JP 2002520018 W Based on WO 2000003011

PRAI **US 1998-92423P 19980710; US 1999-349644 19990708**

IC ICM C12N015-00; C12N015-09; C12N015-12; C12N015-62; **C12P021-04**
ICS **C07K001-12**; **C07K001-18**; C12N015-63

AB WO 200003011 A UPAB: 20000330
NOVELTY - Production of a peptide (I), having isoelectric point (pI) below 5 or over 8, comprises expressing (I), in a host cell, as a fusion protein (FP) with the C-terminal Asp residue of a peptide, attached to (I), recovering FP-containing inclusion bodies (IB), cleaving (FP) under acidic conditions, treating with a non-ionic chaotrope (III), and isolating (I) by ion-exchange chromatography (IEC).

DETAILED DESCRIPTION - In FP, the C-terminal Asp and N-terminus of the attached peptide form a bond that can be cleaved under acidic conditions, (I) has a net charge sufficiently different from that of the peptide and of any unwanted fragments produced by acidic cleavage to allow its separation by IEC, and FP forms IB.

INDEPENDENT CLAIMS are also included for the following:

(1) a method of producing (I), comprising, the novel method where the solubilization of the cleavage products using chaotrope, is replaced by the removal of insoluble cleavage products by ultrafiltration, diafiltration or centrifugation;

(2) vector for expressing FP; and

(3) host cell containing this vector.

ACTIVITY - Cardiant.

MECHANISM OF ACTION - None given.

USE - The method is specifically used to produce b-type natriuretic peptides (Ia) which are useful for treating congestive heart failure, they improve heart function without direct cardiac stimulation, which may cause arrhythmia, and decrease levels of neurohormones which are associated with increased mortality and acceleration of disease progression.

ADVANTAGE - Cleavage of FP in absence of chaotrope results in a soluble (I) which is easily separated from other (insoluble) cleavage products for subsequent purification, which can now be performed without interference from ionic chaotropes.

Dwg.0/7

FS CPI

FA AB; DCN

MC CPI: B04-E08; B04-F01; **B04-N02**; B14-F01; D05-H12C; D05-H12E; **D05-H13**; D05-H14A1; D05-H17C

TECH UPTX: 20000330
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred materials: FP has pI 6-8, particularly 6.5-7.5, and the isolated (I) may be refolded into a biologically active tertiary structure, including formation of disulfide bridges (e.g. by oxidation with iodine). (I) either contains no internal dipeptide sequences that are cleaved by acid, or, if such structures are present, they are cleaved more slowly than the bond in FP holding the parts together. (I) is a b-type natriuretic peptide (Ia). The nonionic chaotrope is particularly urea, used at 3-7 M.
Preferred process: The host cell is Escherichia coli, and IB are suspended at 5-15, particularly 5-8, weight.-volume.% in a solution of pH 1.7-2,2, particularly 1.9-2.1, especially hydrochloric acid, and cleaved for 2-10 hr at 75-**95degreesC**. The solution is then **cooled** to **50degreesC** or less, treated with urea, adjusted to pH 3-7.5, particularly 3.8-4,2, and IEC carried out, e.g. on a sulfopropyl resin. Optionally the product may be purified further, especially by

reverse-phase high-performance liquid chromatography and then IEC again. Preferred vector: This contains regulatory sequence for directing expression of FP, specifically the phoA promoter, and DNA encoding part of a modified chloramphenicol acetyltransferase (CAT) in which enough codons for Lys, Arg and/or His have been replaced by codons for uncharged, or negatively charged, amino acids to result in an FP of pI 6-8. The vector may also contain a codon for Asp at the 3'-end of the modified CAT, attached directly or thorough a linker, and DNA encoding a (I) which has Pro, Gly, Ser, Leu, Ala, Ile or Val at the N-terminus, linked at its 5'-end to the 3'-end of the modified CAT DNA. IN the CAT sequence, at least one amino acid replacement is a hydrophobic residue and the sequence encodes at least 50 residues from the N-terminus of CAT. Optionally oxidizable residues (Cys, Trp and Met) are also replaced in the modified CAT sequence. The vector is assembled by standard methods.

ABEX UPTX: 20000330

EXAMPLE - Plasmid pCB101-1 (ATCC 98774) encodes a b-type natriuretic peptide (Ia) fused to the 3'-end of a modified N-terminal fragment of chloramphenicol acetyltransferase (CAT). A 3.4 kb NdeI-AgeI fragment of this plasmid was ligated to synthetic linkers (sequences reproduced) and plasmid pTH80 (containing a 317 bp AgeI-MluI fragment) selected. A 332 bp CAT-(Ia) sequence was isolated by digestion with NdeI and HindIII and cloned into pTH76 (similar to pTH80 but containing the phoA promoter) to form pTH85. This plasmid was expressed in Escherichia coli (induced by phosphate depletion), then cells harvested, lysed, and inclusion bodies (IB) isolated by centrifugation. IB were resuspended at 10 weight.-volume.% in pH 1.99 aqueous hydrochloric acid, incubated at 80-**90degreesC** for 4.5 hours, then **cooled** and adjusted to pH 2.9. The mixture was treated with solid urea (to 3.5 M) then applied to a column of Whatman Express Ion Exchanger S (sulfoxyethyl resin) and eluted with pH 6.8 phosphate containing 0.5 M sodium chloride. The recovered peptide was oxidized to restore disulfide bonds and purified on a Zorbax Pro 10/150 C8 reverse-phase high-performance liquid chromatography column, to give (Ia) of over 96% purity (yield 406 mg from 4.7 kg wet E. coli cells.

L131 ANSWER 18 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1999-493777 [41] WPIX
DNC C1999-144624
TI DNA encoding human B cell lymphocyte cell surface glycoproteins.
DC B04 D16
IN ARMITAGE, R J; COSMAN, D J; FANSLOW, W C; KUBIN, M; MULLBERG, J H; MULLBERG, J
PA (IMMV) IMMUNEX CORP; (ARMI-I) ARMITAGE R J; (COSM-I) COSMAN D J; (FANS-I) FANSLOW W C; (KUBI-I) KUBIN M; (MULL-I) MULLBERG J
CYC 85
PI WO 9931241 A1 19990624 (199941)* EN 104 C12N015-12 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9920045 A 19990705 (199948) <--
EP 1037991 A1 20000927 (200048) EN C12N015-12 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AU 742757 B 20020110 (200217) C12N015-12 <--
JP 2002508183 W 20020319 (200222) 124 C12N015-09 <--
US 6458350 B1 20021001 (200268) A61K045-00 <--
NZ 505500 A 20021220 (200309) C12N015-12 <--
US 2003147847 A1 20030807 (200358) C08B011-193
US 6653447 B1 20031125 (200378) C07K001-00 <--
US 6774224 B2 20040810 (200453) C07H021-00
US 2004235058 A1 20041125 (200478) G01N033-53

ADT WO 9931241 A1 **WO 1998-US27048 19981217**; AU 9920045 A **AU 1999-20045 19981217**; EP 1037991 A1 **EP 1998-964802 19981217, WO 1998-US27048 19981217**; AU 742757 B **AU 1999-20045 19981217**; JP 2002508183 W **WO 1998-US27048 19981217, JP 2000-539141 19981217**; US 6458350 B1 **Provisional US 1997-69857P 19971217, Provisional US 1998-92946P 19980715, CIP of WO 1998-US27048 19981217, US 2000-532856 20000322**; NZ 505500 A **NZ 1998-505500 19981217, WO 1998-US27048 19981217**; US 2003147847 A1 **Provisional US 1997-69857P 19971217, Provisional US 1998-92946P 19980715, CIP of WO 1998-US27048 19981217, Div ex US 2000-532856 20000322, US 2002-212507 20020805**; US 6653447 B1 **Provisional US 1997-69857P 19971217, Provisional US 1998-92946P 19980715, CIP of WO 1998-US27048 19981217, US 2000-524100 20000313** ; US 6774224 B2 **Provisional US 1997-69857P 19971217, Provisional US 1998-92946P 19980715, CIP of WO 1998-US27048 19981217, Div ex US 2000-532856 20000322, US 2002-212507 20020805**; US 2004235058 A1 **Provisional US 1997-69857P 19971217, Provisional US 1998-92946P 19980715, CIP of WO 1998-US27048 19981217, Div ex US 2000-532856 20000322, Div ex US 2002-212507 20020805**, US 2004-875869 20040623

FDT AU 9920045 A Based on WO 9931241; EP 1037991 A1 Based on WO 9931241; AU 742757 B Previous Publ. AU 9920045, Based on WO 9931241; JP 2002508183 W Based on WO 9931241; NZ 505500 A Based on WO 9931241; US 2003147847 A1 Div ex US 6458350; US 6774224 B2 Div ex US 6458350; US 2004235058 A1 Div ex US 6458350, Div ex US 6774224

PRAI **US 1998-92946P 19980715; US 1997-69857P 19971217; US 2000-532856 20000322; US 2002-212507 20020805; US 2000-524100 20000313**; US 2004-875869 20040623

IC ICM A61K045-00; C07H021-00; **C07K001-00**; C08B011-193; C12N015-09; C12N015-12; G01N033-53

ICS A61K038-17; A61K039-12; C07K014-705; C07K016-22; C07K016-28; C12N001-21; C12N005-10; C12N015-00; C12N015-11; C12N015-62; C12P019-34; **C12P021-00**; **C12P021-08**; C12Q001-02; C12Q001-68

AB WO 9931241 A UPAB: 19991011

NOVELTY - DNA (735, 741 and 950 bp) sequences encoding human B cell lymphocyte cell surface glycoproteins ULBP-1 (244 amino acids), ULBP-2 (246 amino acids) and ULBP-3 (239 amino acids), are new.

All sequences are given in the specification

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) an isolated nucleic acid molecule that hybridizes to either strand of a denatured, double-stranded DNA comprising a DNA as above, under conditions of moderate stringency in 50% formamide and 6 X SSC, at 42 **deg.** C with washing conditions of **60 deg.** C, 0.5 X SSC, 0.1% SDS;

(b) a recombinant vector that directs the expression of a nucleic acid molecule as above;

(c) an isolated polypeptide encoded by a nucleic acid molecule as above;

(d) isolated antibodies that bind to a polypeptide as in (c);

(e) a host cell transfected or transduced with the vector as above;

(f) a method for the production of ULBP-1, -2 or -3 by culturing a host cell as above under conditions promoting expression and recovering the polypeptide from the culture medium;

(g) methods for detecting or killing lymphoma cells;

(h) methods of increasing interferon-gamma (IFN- gamma) or natural killer cell proliferation in vivo;

(i) a method of directly or indirectly increasing cytotoxic T lymphocyte (CTL) activity in vivo; and

(j) a ULBP polypeptide comprising a fragment of the 244, 246 or 239 residue polypeptides, where the fragment is capable of binding to UL-16 or lacks the GPI linkage.

ACTIVITY - Cytostatic; Anti-diabetic.

MECHANISM OF ACTION - None given.

USE - ULBP-1 and -2 bind UL16-Fc. In addition, they bind to a number of human cell types, including mitogen-stimulated human T cells and natural killer (NK) cells. ULBP-Fc proteins bind to K299 cells, an anaplastic lymphoma. The ULBP proteins can therefore be used as markers to detect cancer, to enhance IFN- gamma production, NK cell proliferation and CTL activity, to purify proteins and measure their activity. The polypeptides and their fragments can also be used as delivery and therapeutic agents, for rational drug design, as research reagents, controls for peptide fragmentation, molecular weight/isoelectric focusing markers, identification of unknown proteins and also for preparation of antibodies.

The antibodies can be used in assays to detect the presence of ULBP proteins, in vitro or in vivo, as well as for use in purification of ULBP proteins. The ULBP DNA sequences can be used as probes to identify homologues, to identify human chromosome number 6, to map and identify genes, especially associated with certain diseases, syndromes or other conditions on chromosome 6, as single-stranded sense or antisense oligonucleotides, to inhibit expression of ULBP polypeptides, to help detect defective genes in an individual and for gene therapy.

Diseases, syndromes and conditions associated with human chromosome 6 include Retinitis pigmentosa (6q14-q21), Diabetes mellitus (insulin-dependent) (6q21), progressive pseudorheumatoid arthropathy of childhood (6q22), Muscular dystrophy (congenital merosin-deficient) (6q22-q23), and cardiomyopathy (dilated) (6q23).

Dwg.0/4

FS CPI

FA AB; DCN

MC CPI: **B04-C01**; B04-E01; B04-E02F; B04-E08; B04-F01; B04-G01; **B04-N02**; B12-K04A1; B14-H01; B14-S04; D05-H08; D05-H09; D05-H11; D05-H12A; D05-H12E; **D05-H13**; D05-H14; D05-H17A6; D05-H17C

TECH UPTX: 19991105

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Proteins: The ULBP proteins have molecular weights of about 31 kDa as determined by SDS-PAGE. The proteins may be present in non-glycosylated forms. ULBP-1 was expression cloned from a Namalwa (human B cell lymphoma) cDNA library. This was accomplished by binding to an UL16-Fc fusion protein. UL16 is a type 1 membrane glycoprotein encoded by human cytomegalovirus.

Preferred Host: AThe host cell is selected from a group of bacterial, yeast, plant, and animal cells.

Preferred Antibody: The antibody which binds to the ULBP proteins is a monoclonal antibody.

Preferred Nucleic Acid: An isolated nucleic acid molecule that is:
(i) degenerate from the DNA above as a result of the genetic code; and
(ii) a human ULBP-1, -2 or -3 DNA, an allelic variant or species homologue of the DNA.

ABEX UPTX: 19991105

WIDER DISCLOSURE - ULBP-1 and -2 can be expressed as Fc fusion proteins using an Fc mutein to provide fused polypeptides having 450 and 453 amino acid sequences respectively. The fusion proteins offer the advantage of facile purification by affinity chromatography over Protein A or Protein G columns. ULBP-1 and -2 leucine zipper fusion proteins can also be formed having 270 and 274 amino acid sequences, respectively. The zipper fusion proteins promote the formation of oligomers.

All sequences are given in the specification.

EXAMPLE - ULBP-1 DNA was expressed as a recombinant Fc fusion construct. ULBP-1 DNA encoding the extracellular domain of human ULBP-1 (residues 1-218) was generated by PCR using an upstream primer (P1) containing an

XhoI site and a downstream primer (P2) containing a BglII site.
(1) 5'GCAACTCGAGAGCTCCAGGTCTACAATGGCAG3' (P1); and
(2) 5'GATGAGATCTGGGTTGGGTTGTGCCTGGGGCCAG3' (P2).
The human ULBP-1 DNA fragment was cloned in frame into the pDC409 vector containing a 5' SalI site and the human immunoglobulin Fc region mutein (described in EMBO U. 13:3992, 1994) preceded by a BglII site. The human ULBP-1-Fc fusion polypeptide was produced and purified as described in Fanslow et al. J. Immunol. 149:655, 1995.
For purification, a poly His tag is used to bind the recombinant protein to Nickel-NTA resin. The resin is washed with 30 column volumes of 20 mM NaPO4 pH 7.4 + 300 mM NaCl + 5 mM Imidazole. The recombinant protein is then eluted using increasing concentrations of Imidazole. Fractions are collected and analyzed by SDS-PAGE to identify those containing the recombinant protein.

L131 ANSWER 19 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1997-451985 [42] WPIX
DNC C1997-144217
TI Isolation of proteins from a culture after cultivation - comprises eluting with buffer to fractionate protein, dialysis, filtration and centrifugation.
DC B04 D16
PA (NIQG) NIPPON BCG SEIZO KK
CYC 1
PI JP 09206092 A 19970812 (199742)* 9 C12P021-00 <--
ADT JP 09206092 A **JP 1996-34209 19960130**
PRAI **JP 1996-34209 19960130**
IC ICM **C12P021-00**
ICS A61K049-00; **C07K001-18**; **C07K001-30**; C07K014-35
ICI **C12P021-00**, C12R001:
AB JP 09206092 A UPAB: 19971021
Isolation of proteins from a culture after short use for cultivation of BCG comprises filling the culture a column of different property and eluting by a buffer to fractionate it into several fractions and isolating the fraction containing the protein concentrating fraction and dialysing and repeating the procedure at least twice to purify the proteins, at 40-45 **deg.**C and filtering to remove residual BCG Tokyo and removing proteins of a M.W. lower than 5000 and concentrating culture components, adding ammonium sulphate to **60%** saturation to precipitate the total protein, separating the total protein by centrifugation and supplying the separated protein for the next succeeding step. Also claimed is a reagent for the measurement of delayed type sensitive reaction consisting of one of the above proteins.
ADVANTAGE - The method can recover useful proteins efficiently.
In an example, a culture was filtered and concentrated by ultrafiltration and treated with ammonium sulphate to precipitate the total protein. It was purified by affinity purification using a Phenyl-Sepharose column, a DEAE-Sepharose column containing urea, a Sephacryl column nd a DEAE-Sepharose column containing no urea.
Dwg.0/5
FS CPI
FA AB
MC CPI: **B04-N04**; B12-K04A; **D05-H13**

L131 ANSWER 20 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1995-299565 [39] WPIX
DNC C1995-134129
TI New CD34 antigen binding protein - used for treating blood diseases.
DC B04 D16
PA (NCHK) NICHIREI KK
CYC 1
PI JP 07196691 A 19950801 (199539)* 5 C07K014-47 <--
JP 3267783 B2 20020325 (200222) 5 C07K014-47 <--

ADT JP 07196691 A **JP 1993-349445 19931228**; JP 3267783 B2 **JP 1993-349445 19931228**
FDT JP 3267783 B2 Previous Publ. JP 07196691
PRAI **JP 1993-349445 19931228**
IC ICM C07K014-47
ICS **C07K001-22**; **C12P021-00**
ICI **C12P021-00**, C12R001:
AB JP 07196691 A UPAB: 19951004
A protein having a mol. weight of 14kD and binding to CD34 antigen, is new.
Also claimed are a protein CD34Lp14 having a mol. weight of 14kD which combines specifically with CD34 antigen expressed on a haematopoietic stem cell to give it an activity, and preparation of the protein in which stroma cell is cultured and the culture is treated with CD34 antigen protein column to separate and collect the protein.
USE/ADVANTAGE - The protein is used for treatment of blood diseases.
In an example, human foetal lung-originated normal fibroblast HFL-III was cultured at 37 **deg.**C to 80% confluent. It was washed with DME(-Met, -Cys) and 35S-labelling medium was added and the mixture was cultured at 37 **deg.**C for 16-18 hrs. The cell was washed and dissolved in Lysis medium and the solution was ice-**cooled** for **60** min. and centrifuged. The supernatant was fed to a human I-Fc fraction-Protein G-Sepharose 4Fast Flow column and then to a Protein G-Sepharose 4Fast Flow column and then the eluate was centrifuged. It was reacted with CD34-Ig chimera protein and Protein G-Sepharose was added and the mixture was rotated slowly at 4 **deg.**C for 3 hrs. Protein G-Sepharose was washed and SDS Sample buffer was added and boiled for 10 min. and centrifuged. It was subjected to electrophoresis by SDS-PAGE and the gel was dried and subjected to autoradiography. The presence of the protein was also observed in HFL-I and HUV-EC1. It was suggested the protein is trypsin-resistant.
Dwg.0/3
FS CPI
FA AB
MC CPI: **B04-N04**; D05-H07; D05-H08; **D05-H13**

L131 ANSWER 21 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **1995-011835** [02] WPIX
DNC **C1995-005267**
TI Purificn. of angiotensin converting enzyme-inhibiting peptide(s) - by eliminating insol. material from hydrolysate solution, contacting with synthetic adsorbent and washing with water or brine to recover eluted fraction.
DC B04 D16
PA (NISY) NIPPON SYNTHETIC CHEM IND CO
CYC 1
PI JP 06298794 A 19941025 (199502)* 5 C07K001-14 <--
JP 3430176 B2 20030728 (200351) 5 C07K001-14 <--
ADT JP 06298794 A **JP 1993-114150 19930416**; JP 3430176 B2 **JP 1993-114150 19930416**
FDT JP 3430176 B2 Previous Publ. JP 06298794
PRAI **JP 1993-114150 19930416**
IC ICM **C07K001-14**
ICS **C07K001-12**; C07K003-10; C07K003-20; C07K007-14; C07K015-06; C07K015-08; **C12P021-06**
ICA A61K037-18; A61K037-64
AB JP 06298794 A UPAB: 19950117
In the purificn. of angiotensin-converting enzyme (ACE)-inhibiting peptides which are prepared by hydrolysis of proteins with a proteinase in an aqueous medium, the process involves (1) eliminating insol. material from the hydrolysate solution to make the peptide concentration 10 weight% or higher, (2)
allowing the solution to contact a synthetic adsorbent to recover the void fraction, and (3) washing the synthetic adsorbent with water or brine to

recover the eluated fraction.

The starting proteins are of animal and vegetable origin, e.g. those of fish, shell, swine, bovine and chick meats. The meat is **heated** in water at 50 **deg.**C, the water-soluble portion is eliminated, and the water-insol. portion is used as starting proteins. The proteins may be hydrolysed with a proteinase, e.g. thermolysin, pepsin, trypsin, chymotrypsin, in an aqueous medium, e.g. water, EtOH, MeOH, aqueous solution of Na, K, Mg of Ca chloride, sulphate or carbonate, at 5-90 **deg.**C, pref. 20-70 **deg.**C for 1 min-3 days.

The resulting hydrolysate solution, is applied to centrifugation, filtration or decantation to remove insol. material and the peptide concentration of the solution is adjusted at 10 weight% of higher, pref. 20-50 weight%, by membrane-type vacuum condensation, ultrafiltration or reverse osmosis.

The synthetic adsorbent used includes styrene-divinylbenzene resins (e.g. HP-20, HP-21, SP-825, SP-207, SP-800, SP-850 (mitsubishi Chemical Ind); Amberlite XAD-1, XAD-2, XAD-4, XAD-2000 (Organo)), acrylic resins (e.g. HP1MG, HP2MG (Mitsubishi); XAD-7, XAD-8 (Organo)) and phenol-type resins (e.g. S761 (Sumitomo Chemical)). The peptides may be adsorbed on those resins by a batch operation or by passing through a column of the resin at 5-80 **deg.**C.

USE/ADVANTAGE - Process for purifying bitter peptides which are prepared from proteins and have ACE-inhibiting action. The purified peptides which can be used as antihypertensives or antihypertensive foods may be administered orally or parenterally or rectally at a dose or doses of 0.001-1,000 mg, pref. 0.01-10 mg, a day.

Dwg.0/0

FS CPI
FA AB
MC CPI: B04-N01; **B04-N02**; B14-F02B1; D05-A02C; D05-C11; **D05-H13**

L131 ANSWER 22 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **1994-353766** [44] WPIX
DNC **C1994-160827**
TI Novel tri-peptide inhibitor of angiotensin converting enzyme - obtained by enzymatic hydrolysis of protein, e.g. casein.
DC B04 D16
PA (NISY) NIPPON SYNTHETIC CHEM IND CO
CYC 1
PI JP 06277090 A 19941004 (199444)* 4 C12P021-06 <--
JP 3465921 B2 20031110 (200377) 4 C07K005-08
ADT JP 06277090 A **JP 1993-92551 19930326**; JP 3465921 B2 **JP 1993-92551 19930326**
FDT JP 3465921 B2 Previous Publ. JP 06277090
PRAI **JP 1993-92551 19930326**
IC ICM C07K005-08
ICS A61K037-18; A61K037-64; A61K038-00; A61K038-55; A61P009-12; A61P043-00
ICA **C07K001-12**; C12N009-99; **C12P021-06**
AB JP 06277090 A UPAB: 19941223
Peptide H-Leu-Gly-Tyr-OH is new.

Protein (casein) is hydrolysed with thermolysin (claimed), and obtd. hydrolysate is centrifuged, condensed, and dried to give the peptide.

USE/ADVANTAGE - The peptide is used as inhibitors of angiotensin converting enzyme, useful for therapy of hypertension.

In an example, (5g) was mixed with water (40 ml), and reacted with thermolysin (20 mg) at 37 **deg.** C for 3 hrs. Obtd. reactant was boiled at 100 **deg.** C for 10 min., centrifuged, and condensed. Obtd. condensate was purified by chromatography (ODS-, Ph, and CN-column) to form the peptide. Inhibition activity of the peptide against angiotensin was carried out. Enzyme base of Bz(benzyl)-Gly-His-Leu (100

ul), an enzyme solution of acetone powder of rabbit lung, and the peptide and water were reacted at 37 **deg.** C for 30 mins. 1N-HCl (250 ul) was added thereto and the reactant solution was extracted with ethylacetate. IC50 (u M) of the inhibition of the peptide was 15.5.
Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: **B04-C01A**; B10-B02E; B14-F02B1; **D05-H13**

L131 ANSWER 23 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1992-346223 [42] WPIX
DNC C1992-153917
TI Purificn. of collagen peptide - by contacting peptide prepared by enzymatic decomposition of collagen to solid adsorbent at 20-70 **deg.** C. and pH 2.5-5.
DC B04 D16
PA (ASAK) ASAHI BREWERIES LTD; (HASE) HASEGAWA CO LTD
CYC 1
PI JP 04252194 A 19920908 (199242)* 4 C12P021-06 <--
JP 2509390 B2 19960619 (199629) 4 C12P021-06 <--
ADT JP 04252194 A **JP 1991-25162 19910128**; JP 2509390 B2 **JP 1991-25162 19910128**
FDT JP 2509390 B2 Previous Publ. JP 04252194
PRAI **JP 1991-25162 19910128**
IC ICM **C12P021-06**
ICS A61K037-12; A61K037-18; **C07K001-22**; C07K003-18
ICA A23J003-34; A61K038-00
AB JP 04252194 A UPAB: 19970502
Purificn. of collagen peptide (I) comprises contacting a peptide prepared by enzymatic decomposition of collagen to a solid absorbent at a **temp**. of 20 to 70 **deg.**C under acid conditions of pH 2.5 to 5.
USE/ADVANTAGE - The purified (I) has no bad odour, is colourless and has good taste and gives no turbidity to a drink when added to it.
In an example, 1kg of a commercial gelatin powder is dispersed in 9 kg pure water and dissolved in it by **heating** to 40 to 50 **deg.**C. It is sterilised at 85 **deg.**C for 15 min. and **cooled** to 50 **deg.**C 50g 10% aqueous solution of Collolase RN (Rohm Co.) is added to it and decomposed at 50 **deg.**C at a pH of 6.8 under stirring for 5 hrs. The resultant liquid is **heated** at 85 **deg.**C for 15 min. to inactivate the enzyme and filtered through a filter paper and spray dried by a usual method to give 930 g crude (I). 200g of it is dissolved in 800g pure water at **60 deg**.C. 20g active carbon is added and stirred at **60 deg.**C for 1 hr. and the solution is filtered to give 960g 20% aqueous solution of pure (I). The same procedure is repeated except that 7g citric acid is added to a pH of 3.6 to give 980 g 20% aqueous solution, of pure (I). The latter has lower in odour and colour than the former and shows no turbidity in a drink containing 75g 80% (I) solution 80g soft sugar and 3.5g citric acid in 1 litre
Dwg.0/0
FS CPI
FA AB
MC CPI: **B04-C01**; B12-J01; D03-H01J; **D05-H13**

L131 ANSWER 24 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1988-260528 [37] WPIX
DNC C1988-116045
TI CGF extracted from bovine thymus - has high cell metabolic activity, and is used to treat hepatitis, gastrointestinal ulcer, etc..
DC B04 D16
PA (ICHP) ICHIMARU PHARCOS INC
CYC 1

PI JP 63188698 A 19880804 (198837)* 5 <--
JP 07020996 B2 19950308 (199514) 6 C07K014-47 <--
ADT JP 63188698 A **JP 1987-19084 19870129**; JP 07020996 B2 **JP 1987-19084 19870129**
FDT JP 07020996 B2 Based on JP 63188698
PRAI **JP 1987-19084 19870129**
IC A61K035-24; A61K037-02; A61K039-00; C07K003-02; C07K015-06; **C12P021-00**
ICM C07K014-47
ICS A61K037-02; A61K039-00; **C07K001-16**; **C07K001-22**; **C07K001-30**; C07K003-02; C07K015-06
ICA A61K035-24; A61K038-00; **C12P021-00**
AB JP 63188698 A UPAB: 19930923
CGF is extracted from bovine thymus where it is H2O soluble protein of presumed m.w. 46,000, i.p. about 6.0-6.5.

As starting material, bovine thymus is used. It is minced, homogenate at low **temperature**, and H2O, NaCl solution or common buffer is added and mixture is allowed to stand for 6-24 hours. The supernatant obtd. by centrifugation is treated by adding (NH4)2SO4 at 40% saturation, then the supernatant is taken by centrifugation. To this, (NH4)2SO4 is added at **60%** saturated concentration The produced ppte. is purified by combination of gel filtration and ion exchange chromatography. Obtd. H2O soluble protein has presumed m.w. 46,000, and i.p. about 6.0-6.5. The ppte. is **heat** treated at **60 deg.**C for 10 hours, or the H2O soluble protein purified by combination of gel filtration and ion exchange chromatography is added to (NH4)2SO4 **60%** saturated concentration solution, and produced ppte. is **heat** treated at **60 deg.**C for 10 hours to obtain stable and virus inactivated CGF.

USE/ADVANTAGE - The protein has high cell metabolic activity directly. Virusis inactivated and cell growth activating effect against cell is residued at 80-90%. It is useful for treatment of hepatitis, gastro-intestinal ulcer, etc. or additive for tissue culture.
0/0
FS CPI
FA AB
MC CPI: **B04-B04A6**; B04-B04J; B11-B; B12-A06; B12-E08; B12-G02; D05-H08; **D05-H13**

L131 ANSWER 25 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1988-260527 [37] WPIX
DNC C1988-116044
TI CGF with high cell metabolic activating effect - obtd. by extraction from bovine spleen, for inactivation of virus.
DC B04 D16
PA (ICHP) ICHIMARU PHARCOS INC
CYC 1
PI JP 63188697 A 19880804 (198837)* 6 <--
JP 07020995 B2 19950308 (199514) 6 C07K014-47 <--
ADT JP 63188697 A **JP 1987-19083 19870129**; JP 07020995 B2 **JP 1987-19083 19870129**
FDT JP 07020995 B2 Based on JP 63188697
PRAI **JP 1987-19083 19870129**
IC A61K035-28; A61K037-02; A61K039-00; C07K003-02; C07K015-06; **C12P021-00**
ICM C07K014-47
ICS A61K037-02; A61K039-00; **C07K001-16**; **C07K001-22**; **C07K001-30**; C07K003-02; C07K015-06
ICA A61K035-28; A61K038-00; **C12P021-00**
AB JP 63188697 A UPAB: 19930923
CGF is extracted from bovine spleen, where it is H2O soluble protein of presumed m.w. 41,000, i.p. about 6.0-6.5.

As starting material, bovine spleen is used. This is minced, homogenised at a low **temperature**, H2O, NaCl aqueous solution or various

common buffer is added, still standing for 6-24 hours, centrifuged and the supernatant obtd. by centrifugation is separated Then, (NH4)2SO4 is added to the supernatant to give 40% saturation, centrifuged, and the obtd. supernatant is treated by (NH4)2SO4 to give **60%** saturated concentration; the ppte. is collected and purified by combination of gel filtration, ion exchange chromatography, and H2O soluble protein of presumed m.w. 41,000, i.p. about 6.0-6.5 is obtd. The ppte. obtd. by **60%** saturated concentration (NH4)2SO4, is **heated** at **60 deg.**C for 10 hours, or the purified H2O soluble protein by combination of gel filtration and ion exchange chromatography is added in (NH4)2SO4 **60%** saturated concentration solution, for precipitation, the ppte. is **heated** treated at **60 deg.**C for 10 hours to obtain stable active and virus inactivated CGF.

USE/ADVANTAGE - The protein has high direct cell metabolic activating effect. Inactivation of virus can be achieved, and cell growth accelerating activity of 80-90% can be obtd.

0/0

FS CPI
FA AB
MC CPI: **B04-B04A6**; B04-B04J; B11-B; B12-A06; **D05-H13**

L131 ANSWER 26 OF 26 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1981-62337D [35] WPIX
TI B30 threonine human insulin ester production - by trans-peptisation of e.g. pig insulin with threonine ester in presence of trypsin.
DC B04
IN **MARKUSSEN, J**
PA (NOVO) NOVO IND AS
CYC 23
PI

BE 887480	A	19810811	(198135)*	37	
GB 2069502	A	19810826	(198135)		
FR 2475542	A	19810814	(198138)		
NL 8100624	A	19810901	(198139)		
NO 8100443	A	19810907	(198140)		
SE 8100928	A	19810914	(198140)		
FI 8100385	A	19810930	(198143)		
DK 8000574	A	19811005	(198144)		
DK 8100540	A	19811005	(198144)		
DE 3104949	A	19811126	(198149)		
JP 56135452	A	19811022	(198149)		
ZA 8100898	A	19820122	(198217)		
PT 72485	A	19820426	(198220)		
US 4343898	A	19820810	(198234)		
DE 3153088	A	19831110	(198346)		
CA 1162868	A	19840228	(198413)		
DE 3104949	C	19840426	(198418)		
GB 2069502	B	19840808	(198432)		
NL 178797	B	19851216	(198602)		
CH 655949	A	19860530	(198625)		
SE 451143	B	19870907	(198738)		
JP 02011240	B	19900313	(199014)		
IT 1195038	B	19880928	(199108)		
AT 8100636	A	19941215	(199505)	C07K001-02	<--
AT 399881	B	19950615	(199529)	C07K001-02	<--

ADT GB 2069502 A GB 1981-4114 19810210; NL 8100624 A NL 1981-624 19810210; DE 3104949 A DE 1981-3104949 19810211; JP 56135452 A JP 1981-17580 19810210; AT 8100636 A AT 1981-636 19810211; AT 399881 B AT 1981-636 19810211
FDT AT 399881 B Previous Publ. AT 8100636
PRAI DK 1980-574 19800211; DK 1980-3662 19800828
IC A61K000-00; C07C103-52; **C12P021-04**
ICM **C07K001-02**
ICS A61K000-00; C07C103-52; C07K007-40; **C12P021-04**
AB BE 887480 A UPAB: 19930915

Production of esters (I) of B30-Thr human insulin, or salts or complexes, comprises transpeptidation of a suitable insulin cpd. (II), or its salts or complexes, with L-threonine ester (III), or its salt, in a mixture of water, water miscible organic solvent and trypsin, opt. in presence of acid. The water content of the medium is below 50(pref. 10-40)volume% and **temperature** is below 50 **deg.**C., especially between room **temp**. and 0 **deg.**C. The (III) concentration is pref. over 0.1M and the mixture contains 0-10, esp.0.5-5 ewuiv. (III). (II) is especially relatively impure pig insulin (PI), and the (III): (II) mole ratio is over 5:1. (I), where the ester gp. is other than methyl, or tert, butyl, are new.

(I) are intermediates, by removal of the ester function, for human insulin (HI). They can be prepared on a large scale from the readily available PI(which differs from HI in having a B30-Ala instead of B-30 Thr residue). (I) yields of over 90% can be achieved.

FS CPI
FA AB
MC CPI: B04-B02D
ABEQ DE 3104949 C UPAB: 19930915

Prepn. of threonine B30-insulinate or its salts or complexes comprises reaction of L-threonine esters of formula Thr(R')OR, (where R is a protective group for the COOH group and R' is a protective group for active H or OH), or their salts with human or other insulin or its salts or complexes having aminoacid sequences A1-A21 and B1-B29, in the presence of a protease and an acid, in a mixt. of a water-miscible organic solvent and water (less than 50 (10-40) vol. % aq.), at 0-50 (37) **deg.** C.

Suitable enzymes are opt. modified trypsin and Achromobacter lyticus protease. Pref. solvents are 1-3 C alcohols, glycol, Me2CO, dioxane, THF, MeCN and amides. The prods. are used for the treatment of diabetes mellitus.

ABEQ GB 2069502 B UPAB: 19930915

A process for preparing threonine B30 esters of human insulin or a salt or complex thereof, characterised by transpeptidizing an insulin compound or a salt or complex thereof convertible therinto with an L-threonine ester or a salt thereof in a mixture of water, a water miscible organic solvent, and trypsin type protease, the content of water in the reaction mixture being less than 50 per cent (volume/volume), and the reaction **temperature** being below 50 **deg.**C., and in the optional presence of an acid.

=> d his

(FILE 'HOME' ENTERED AT 09:11:53 ON 02 MAR 2005)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 09:11:58 ON 02 MAR 2005
L1 1 S US20040137571/PN OR (US2003-719601# OR US2002-430748# OR DK20
E MARKUSSEN J/AU
L2 124 S E3-E6
E DIERS I/AU
L3 33 S E3-E6
L4 2723 S (NOVO(L)NORDISK?)/PA,CS
SEL RN L1

FILE 'REGISTRY' ENTERED AT 09:17:24 ON 02 MAR 2005
L5 10 S E1-E10
L6 9 S L5 NOT ETHANOL/CN
E INSULIN/CN
E INSULIN (HUMAN)/CN
L7 1 S E3
L8 4024 S INSULIN (L) HUMAN
L9 3121 S L8 AND PROTEIN/FS

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L10        1911 S L9 AND INSULIN()HUMAN/INS.HP
L11        1210 S L9 NOT L7,L10
L12         377 S L11 NOT INSULIN LIKE GROWTH FACTOR
L13         353 S L12 NOT INSULIN LIKE
L14         350 S L13 NOT ENZYME
L15         299 S L14 NOT GENE
L16         293 S L15 NOT INSULIN RESPONSIVE
L17         293 S L16 NOT DNA
L18         226 S L17 AND INSULIN/INS.HP
L19         217 S L18 NOT KINASE
L20         214 S L19 NOT CCS/CI
L21         212 S L20 NOT ANTI INSULIN
L22         209 S L21 NOT INSULIN PROMOTER
L23         179 S L22 NOT FUSION PROTEIN
L24         178 S L23 NOT INSULINASE
L25        7545 S INSULIN NOT L6,L7,L24
L26        5905 S L25 NOT NUCLEIC/FS

     FILE 'HCAPLUS' ENTERED AT 09:32:54 ON 02 MAR 2005
               E FERMENTATION/CT
L27        5515 S E7,E9,E15
               E E3+ALL
L28       91162 S E4+NT
               E FERMENTATION/SC,SX
L29      150611 S E3,E4
L30      202504 S FERMENT?/SC,SX
L31      217709 S L27-L30
               E TEMPERATURE/CT
L32         602 S E3-E6,E9 AND L31
               E E3+ALL
L33         765 S E1+NT AND L31
               E E57+ALL
L34         606 S E1+NT AND L31
               E E12+ALL
L35         347 S E7+NT AND L31
               E E33+ALL
L36          41 S E1+NT AND L31
               E TEMPERATURE/CT
L37           0 S E13+NT AND L31
L38        2192 S E21+NT AND L31
L39        3875 S L32-L38
               E COOL/CT
L40          72 S E33,E35 AND L31
               E E33+ALL
L41         477 S E7+NT AND L31
L42           1 S E30+NT AND L31
               E E6+ALL
L43         899 S E6+NT AND L31
L44        4359 S L39-L43
               E PRECEIPATATION/CT
               E PRECIPATATION/CT
               E PRECIPITATION/CT
L45           0 S E3 AND L44
L46           0 S E25 AND L44
L47           0 S E23 AND L44
               E E5+ALL
L48          74 S E3,E4,E2+NT AND L44
               E E38+ALL
L49           0 S E1 AND L44
               E SULUBILITY/CT
               E SOLUBILITY/CT
L50          39 S (E3+OLD,NT OR E7+OLD,NT OR E8 OR E9+OLD,NT OR E16+OLD,NT) AND
L51           8 S L48 AND L50
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L52          12 S L6,L7,L24 AND L44
L53           6 S L26 AND L44
L54          16 S L52,L53
L55          30 S L2,L3 AND L31
L56           1 S L55 AND L44
L57          29 S L55 NOT L56
                SEL DN AN 19
L58           1 S L57 AND E1-E3
L59           8 S PEPTIDE#/CW (L) TFF
L60           1 S L44 AND (TREFOIL FACTOR FAMILY OR TFF OR L59)
                E INTERLEUKINS/CT
                E E3+ALL
L61          16 S E7,E6+NT AND L44
                E ALBUMIN/CT
L62           0 S E3,E11 AND L44
                E E46+ALL
L63          35 S E2+NT AND L44
L64           3 S L54,L61,L63 AND L48,L50
L65        2333 S L44 AND DEGREE
L66          41 S L65 AND L48,L50
L67          25 S L65 AND L54,L61,L63
L68         101 S L66,L67,L54,L56,L58,L60,L61,L63,L64 AND L1-L4,L27-L67
L69          83 S L68 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L70          78 S L69 AND (DEGREE OR TEMPERATURE OR HEAT? OR COOL? OR THERMAL?
L71           5 S L69 NOT L70
                SEL DN AN 3
L72           1 S L71 AND E1-E3
L73          45 S L70 AND (?PROTEIN? OR ?PEPTIDE?)
L74          49 S L70 AND (?INSULIN? OR EXENDIN OR GLUCAGON OR TFF OR TREFOIL F
L75          60 S L73,L74
L76          18 S L70 NOT L75
                SEL DN AN 1 3 7 10 14
L77           5 S L76 AND E4-E18
L78           9 S L75 AND 60
                SEL DN AN 2 3 4 6 8 9
L79           3 S L78 NOT E19-E36
L80          51 S L75 NOT L76-L79
L81           4 S L80 AND 40
L82          47 S L80 NOT L81
                SEL DN AN 5 6 9 10 13 15 17 20 21 24 31 33 35 38 43 45
L83          16 S E37-E84 AND L82
L84          29 S L72,L77,L79,L81,L83 AND L1-L4,L27-L83

     FILE 'HCAPLUS' ENTERED AT 10:33:38 ON 02 MAR 2005
                SEL HIT RN L84

     FILE 'REGISTRY' ENTERED AT 10:34:18 ON 02 MAR 2005
L85          10 S E85-E94 AND L5-L26

     FILE 'BIOSIS' ENTERED AT 10:35:01 ON 02 MAR 2005
                E MARKUSSEN J/AU
L86         109 S E3,E4
                E DIERS I/AU
L87          25 S E3-E5
L88         129 S L86,L87
L89           4 S L88 AND ?FERMENT?
L90           4 S L88 AND 32500/CC
L91           7 S L89,L90
L92          52 S L88 AND 10054/CC
L93         108 S L88 AND 10064/CC
L94           3 S L92,L93 AND L91

     FILE 'WPIX' ENTERED AT 10:38:26 ON 02 MAR 2005
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L95           1 S L1
L96        3405 S C07K001/IPC AND C12P021/IPC
L97           1 S L95 AND (N13?(S)N16?)/M0,M1,M2,M3,M4,M5,M6
L98         237 S L96 AND N512/M0,M1,M2,M3,M4,M5,M6
L99         238 S L96 AND N513/M0,M1,M2,M3,M4,M5,M6
L100        453 S L96 AND (DEG OR DEGREE?)/BIX
L101        407 S L96 AND (TEMPERATURE OR HEAT? OR COOL? OR THERMAL? OR HOT OR
L102        896 S L98-L101
L103        164 S L102 AND D05-H13/MC
L104        531 S L102 AND (B04-C01? OR C04-C01? OR B04-H02? OR C04-H02? OR B04
L105         87 S L103 AND L104
L106         84 S L105 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L107         19 S L106 AND 60/BIX
L108         44 S L106 AND L100
L109         35 S L106 AND L98,L99
L110         25 S L106 AND TEMPERATURE/BIX
L111         18 S L107 AND L108-L110
L112         16 S L111 AND L100
L113          3 S L107,L111 NOT L112
L114         15 S L110 NOT L111-L113
                SEL DN AN 5 L114
L115          1 S L114 AND E1-E2
L116         50 S L106 NOT L110-L115
L117         15 S L116 AND ?DEGREE?/BIX
                SEL DN AN 13 15
L118          2 S E3-E6 AND L117
L119          6 S L116 AND DEG/BIX NOT L117
                SEL DN AN 2 3
L120          2 S L119 AND E7-E10
L121         29 S L116 NOT L117-L120
L122          0 S L121 AND TEMPERATURE/BIX
L123         21 S L112,L115,L118,L120
                E DIERS N/AU
L124          4 S E3
                E DIERS I/AU
L125         10 S E3
                E MARKUSSEN J/AU
L126         18 S E3
L127          5 S L96 AND L124-L126
L128         25 S L123,L127
L129         20 S L124-L126 NOT L128
                SEL DN AN 3
L130          1 S L129 AND E1-E2
L131         26 S L128,L130 AND L95-L130

     FILE 'WPIX' ENTERED AT 11:29:30 ON 02 MAR 2005

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                   STN Express with Discover!
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 NEWS  5  NOV 30   PHAR reloaded with additional data
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 NEWS  8  DEC 15   MEDLINE update schedule for December 2004
 NEWS  9  DEC 17   ELCOM reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  10 DEC 17   COMPUAB reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  11 DEC 17   SOLIDSTATE reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  12 DEC 17   CERAB reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  13 DEC 17   THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
 NEWS  14 DEC 30   EPFULL: New patent full text database to be available on STN
 NEWS  15 DEC 30   CAPLUS - PATENT COVERAGE EXPANDED
 NEWS  16 JAN 03   No connect-hour charges in EPFULL during January and
                   February 2005
 NEWS  17 FEB 25   CA/CAPLUS - Russian Agency for Patents and Trademarks
                   (ROSPATENT) added to list of core patent offices covered
 NEWS  18 FEB 10   STN Patent Forums to be held in March 2005
 NEWS  19 FEB 16   STN User Update to be held in conjunction with the 229th ACS
                   National Meeting on March 13, 2005
 NEWS  20 FEB 28   PATDPAFULL - New display fields provide for legal status
                   data from INPADOC
 NEWS  21 FEB 28   BABS - Current-awareness alerts (SDIs) available
 NEWS  22 FEB 28   MEDLINE/LMEDLINE reloaded
 NEWS  23 MAR 02   GBFULL: New full-text patent database on STN

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               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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FILE 'HOME' ENTERED AT 12:27:15 ON 02 MAR 2005

=> file medline, uspatful, dgene, embase, wpids, fsta, jicst, japio, wpix,
biotechds, biosis, biobusiness
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

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FILE 'USPATFULL' ENTERED AT 12:27:55 ON 02 MAR 2005
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=> s purification procees and (fermentation product) and (temperature)
L1            0 PURIFICATION PROCEES AND (FERMENTATION PRODUCT) AND (TEMPERATURE
                )

=> s purification process and (60 degrees)
L2           87 PURIFICATION PROCESS AND (60 DEGREES)

=> s l2 and (60 degrees to 90 degrees)
  10 FILES SEARCHED...
L3            0 L2 AND (60 DEGREES TO 90 DEGREES)

=> s l2 and (cooling to 59 degrees or 58 degrees or 57 degrees or 56 degrees or 55
degrees or 40 degrees)
   8 FILES SEARCHED...
L4            7 L2 AND (COOLING TO 59 DEGREES OR 58 DEGREES OR 57 DEGREES OR
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56 DEGREES OR 55 DEGREES OR 40 DEGREES)

=> d l4 ti abs ibib tot

L4 ANSWER 1 OF 7 USPATFULL on STN
TI **Purification process** for hexafluoroethane products
AB The disclosure relates to removing impurities from hexafluoroethane (CF.sub.3 CF.sub.3), also known as Perfluorocarbon 116 (PFC-116) or Fluorocarbon 116 (FC-116), by using azeotropic distillation such that an overhead product consisting essentially of HCl-hexafluoroethane is formed, optionally combined with a phase separation step to break the HCl-hexafluoroethane azeotropic or azeotrope-like composition thereby permitting recovery of substantially pure hexafluoroethane. Unreacted hydrogen fluoride (HF) may be removed from hexafluoroethane during the above azeotropic distillation with HCl or alternatively by an azeotropic distillation wherein an HF-hexafluoroethane azeotropic or azeotrope-like composition exits overhead and substantially pure HF exits in the bottoms stream.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2001:59851 USPATFULL
TITLE: **Purification process** for hexafluoroethane products
INVENTOR(S): Miller, Ralph Newton, Newark, DE, United States
Deschere, Mark Richard, Newark, DE, United States
Mahler, Barry Asher, Glen Mills, PA, United States
Muthu, Olagappan, Newark, DE, United States
PATENT ASSIGNEE(S): E. I. du Pont de Nemours and Company, Wilmington, DE, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6221830	B1	20010424
APPLICATION INFO.:	US 1997-842843		19970417 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1994-309376, filed on 20 Sep 1994, now patented, Pat. No. US 5718807
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Gupta, Yogendra
ASSISTANT EXAMINER: Webb, Gregory E.
LEGAL REPRESENTATIVE: Shipley, James E.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Figure(s); 18 Drawing Page(s)
LINE COUNT: 1883
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 2 OF 7 USPATFULL on STN
TI **Purification process** for hexafluoroethane products
AB The disclosure relates to removing impurities from hexafluoroethane (CF.sub.3 CF.sub.3), also known as Perfluorocarbon 116 (PFC-116) or Fluorocarbon 116 (FC-116), by using azeotropic distillation such that an overhead product consisting essentially of HCl-hexafluoroethane is formed, optionally combined with a phase separation step to break the HCl-hexafluoroethane azeotropic or azeotrope-like composition thereby permitting recovery of substantially pure hexafluoroethane. Unreacted hydrogen fluoride (HF) may be removed from hexafluoroethane during the above azeotropic distillation with HCl or alternatively by an azeotropic distillation wherein an HF-hexafluoroethane azeotropic or azeotrope-like composition exits overhead and substantially pure HF exits in the bottoms stream.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1998:22456 USPATFULL

TITLE: **Purification process** for hexafluoroethane products

INVENTOR(S): Miller, Ralph Newton, Newark, DE, United States
Deschere, Mark Richard, Newark, DE, United States
Mahler, Barry Asher, Glen Mills, PA, United States
Muthu, Olagappan, Newark, DE, United States

PATENT ASSIGNEE(S): E. I. du Pont de Nemours and Company, Wilmington, DE, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5723699		19980303
APPLICATION INFO.:	US 1997-789173		19970124 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-455883, filed on 31 May 1995, now abandoned which is a continuation of Ser. No. US 1994-309376, filed on 20 Sep 1994

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Siegel, Alan
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Figure(s); 18 Drawing Page(s)
LINE COUNT: 1981
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 3 OF 7 USPATFULL on STN
TI **Purification process** for hexafluoroethane products
AB The disclosure relates to removing impurities from hexafluoroethane (CF.sub.3 CF.sub.3), also known as PerFluoroCarbon 116 (PFC-116) or FluoroCarbon 116 (FC-116), by using azeotropic distillation such that an overhead product containing an HCl-hexafluoroethane is formed, optionally combined with a phase separation step to break the HCl-hexafluoroethane azeotropic or azeotrope-like composition thereby permitting recovery of substantially pure hexafluoroethane. Unreacted hydrogen fluoride (HF) may be removed from hexafluoroethane during the above azeotropic distillation with HCl or alternatively by an azeotropic distillation wherein an HF-hexafluoroethane azeotropic or azeotrope-like composition exits overhead and substantially pure HF exits in the bottoms stream.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1998:16984 USPATFULL
TITLE: **Purification process** for hexafluoroethane products

INVENTOR(S): Miller, Ralph Newton, Newark, DE, United States
Deschere, Mark Richard, Newark, DE, United States
Mahler, Barry Asher, Glen Mills, PA, United States
Muthu, Olagappan, Newark, DE, United States

PATENT ASSIGNEE(S): E. I. du Pont de Nemours and Company, Wilmington, DE, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5718807		19980217
APPLICATION INFO.:	US 1994-309376		19940920 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Manoharan, Virginia
LEGAL REPRESENTATIVE: Shipley, James E.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1,3
NUMBER OF DRAWINGS: 18 Drawing Figure(s); 18 Drawing Page(s)
LINE COUNT: 2023
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 4 OF 7 USPATFULL on STN
TI Method for purification of calcium carbonate
AB A method for lowering the iron content of calcium carbonate is disclosed. The method involves addition of an iron chelating agent to an aqueous calcium carbonate slurry, reducing the pH of the aqueous calcium carbonate by employing carbon dioxide containing gas, while maintaining the aqueous calcium carbonate slurry at an elevated temperature. The slurry is stirred, filtered, washed and dried. The calcium carbonate product resulting from the process of the present invention has a reduced iron content.

Calcium carbonate produced according to the method of this invention is particularly suitable for use as food or pharmaceutical additives and may also be useful as a filler in papermaking processes or as additives in plastic products.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	97:109465 USPATFULL		
TITLE:	Method for purification of calcium carbonate		
INVENTOR(S):	Drummond, Donald Kendall, Glenmoore, PA, United States		
PATENT ASSIGNEE(S):	Minerals Technologies Inc., New York, NY, United States (U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5690897		19971125
APPLICATION INFO.:	US 1994-343002		19941121 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Langel, Wayne		
LEGAL REPRESENTATIVE:	Powell, Marvin J., Morris, Terry B.		
NUMBER OF CLAIMS:	10		
EXEMPLARY CLAIM:	1		
LINE COUNT:	279		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 5 OF 7 USPATFULL on STN
TI Purified Bacillus licheniformis PWD-1 keratinase
AB A substantially pure keratinaceous material-degrading B. licheniformis PWD-1 enzyme is disclosed. The substantially pure enzyme is characterized by a molecular weight of 33 kiloDaltons, an isoelectric point of 7.25, an optimum pH of 7.5, an optimum temperature of 45°-50° C., and thermal stability at low temperatures.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	92:102998 USPATFULL		
TITLE:	Purified Bacillus licheniformis PWD-1 keratinase		
INVENTOR(S):	Shih, Jason C. H., Cary, NC, United States Williams, C. Michael, Cary, NC, United States		
PATENT ASSIGNEE(S):	North Carolina State University, Raleigh, NC, United States (U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5171682		19921215
APPLICATION INFO.:	US 1991-769553		19911001 (7)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1990-581681, filed on 13 Sep 1990, now patented, Pat. No. US 5063161 which is a continuation of Ser. No. US 1988-175476, filed on 31 Mar 1988, now patented, Pat. No. US 4959311, issued on 25 Sep 1990		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		

PRIMARY EXAMINER: Wax, Robert A.
ASSISTANT EXAMINER: Hendricks, Keith D.
LEGAL REPRESENTATIVE: Bell, Seltzer, Park & Gibson
NUMBER OF CLAIMS: 1
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 758
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 6 OF 7 USPATFULL on STN
TI Electrolytic process including recovery and condensation of high pressure chlorine gas
AB Discloses the electrolysis of aqueous alkali metal halides while maintaining the anolyte compartment at an elevated pressure, whereby to recover chlorine therefrom at a superatmospheric partial pressure. The superatmospheric partial pressure chlorine gas is recovered from the cell and condensed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 83:3970 USPATFULL
TITLE: Electrolytic process including recovery and condensation of high pressure chlorine gas
INVENTOR(S): Graybill, Wilmer B., Pittsburgh, PA, United States
Korach, Malcolm, Pittsburgh, PA, United States
PATENT ASSIGNEE(S): PPG Industries, Inc., Pittsburgh, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4370209		19830125
APPLICATION INFO.:	US 1981-233427		19810211 (6)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1979-14466, filed on 23 Feb 1979, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Andrews, R. L.
LEGAL REPRESENTATIVE: Goldman, Richard M.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 465
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 7 OF 7 USPATFULL on STN
TI Hop extracts and method of preparation
AB Hop extracts useful in the preparation of anactinic or light stable malt beverages are obtained by a method which does not use organic solvents. The extracts are obtained by first treating a crude hop extract containing humulone with an aqueous reducing solution, heating the resulting mixture to form reduced isohumulone, acidifying the reaction mixture to form an aqueous phase and an organic phase, and then adjusting the temperature to facilitate the separation of the two phases. The organic phase which is obtained contains the desired isomerized and reduced humulone and it can be used per se as an anactinic brew kettle flavoring additive for beer or ale. In a preferred embodiment, the organic phase is further treated with an amount of an aqueous KOH solution sufficient to neutralize the reduced isohumulone and to form both an aqueous phase and a solid phase. The aqueous phase which contains reduced isohumulone of about 90+% purity can be used as an anactinic post-kettle additive and the solid phase which contains the remainder of the reduced isohumulone and other hop constituents can be used as an anactinic brew kettle additive.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 82:17672 USPATFULL

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TITLE:                    Hop extracts and method of preparation
INVENTOR(S):              Goldstein, Henry, Brookfield, WI, United States
                          Fly, Walter, Milwaukee, WI, United States
                          Ting, Patrick, Brookfield, WI, United States
                          Chicoye, Etzer, Wauwatosa, WI, United States
PATENT ASSIGNEE(S):       Miller Brewing Company, Milwaukee, WI, United States
                          (U.S. corporation)

                               NUMBER         KIND    DATE
                          ---------------- ------ --------
PATENT INFORMATION:       US 4324810               19820413
APPLICATION INFO.:        US 1980-154577           19800529  (6)
DOCUMENT TYPE:            Utility
FILE SEGMENT:             Granted
PRIMARY EXAMINER:         Halper, Robert
LEGAL REPRESENTATIVE:     Quarles & Brady
NUMBER OF CLAIMS:         9
EXEMPLARY CLAIM:          1
NUMBER OF DRAWINGS:       1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT:               471
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> d his

     (FILE 'HOME' ENTERED AT 12:27:15 ON 02 MAR 2005)

     FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS, JAPIO,
     WPIX, BIOTECHDS, BIOSIS, BIOBUSINESS' ENTERED AT 12:27:55 ON 02 MAR 2005
L1             0 S PURIFICATION PROCEES AND (FERMENTATION PRODUCT) AND (TEMPERAT
L2            87 S PURIFICATION PROCESS AND (60 DEGREES)
L3             0 S L2 AND (60 DEGREES TO 90 DEGREES)
L4             7 S L2 AND (COOLING TO 59 DEGREES OR 58 DEGREES OR 57 DEGREES OR

=> s purification process adj (heating or cooling)
MISSING OPERATOR 'ADJ (HEATING'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s purification process and (heating or cooling)
   9 FILES SEARCHED...
L5          5656 PURIFICATION PROCESS AND (HEATING OR COOLING)

=> s l5 and (59 degrees or 60 degrees)
L6            60 L5 AND (59 DEGREES OR 60 DEGREES)

=> s l2 and protein
L7            23 L2 AND PROTEIN

=> d l7 ti abs ibib tot

L7   ANSWER 1 OF 23      MEDLINE on STN
TI   Purification and investigation of some kinetic properties of
     glucose-6-phosphate dehydrogenase from parsley (Petroselinum hortense)
     leaves.
AB   In this study, glucose-6-phosphate dehydrogenase (D-glucose-6-phosphate:
     NADP+ oxidoreductase, EC 1.1.1.49; G6PD) was purified from parsley
     (Petroselinum hortense) leaves, and analysis of the kinetic behavior and
     some properties of the enzyme were investigated.  The purification
     consisted of three steps: preparation of homogenate, ammonium sulfate
     fractionation, and DEAE-Sephadex A50 ion exchange chromatography.  The
     enzyme was obtained with a yield of 8.79% and had a specific activity of
     2.146 U (mg protein)(-1).  The overall purification was about
     58-fold.  Temperature of +4 degrees C was maintained during the
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purification process. Enzyme activity was spectrophotometrically measured according to the Beutler method, at 340 nm. In order to control the purification of enzyme, SDS-polyacrylamide gel electrophoresis was carried out in 4% and 10% acrylamide for stacking and running gel, respectively. SDS-polyacrylamide gel electrophoresis showed a single band for enzyme. The molecular weight was found to be 77.6 kDa by Sephadex G-150 gel filtration chromatography. A **protein** band corresponding to a molecular weight of 79.3 kDa was obtained on SDS-polyacrylamide gel electrophoresis. For the enzymes, the stable pH, optimum pH, and optimum temperature were found to be 6.0, 8.0, and **60 degrees** C, respectively. Moreover, KM and Vmax values for NADP+ and G6-P at optimum pH and 25 degrees C were determined by means of Lineweaver-Burk graphs. Additionally, effects of streptomycin sulfate and tetracycline antibiotics were investigated for the enzyme activity of glucose-6-phosphate dehydrogenase in vitro.

ACCESSION NUMBER: 2002328945 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12071647
TITLE: Purification and investigation of some kinetic properties of glucose-6-phosphate dehydrogenase from parsley (Petroselinum hortense) leaves.
AUTHOR: Coban T Abdul Kadir; Ciftci Mehmet; Kufrevioglu O Irfan
CORPORATE SOURCE: Faculty of Erzincan Education, Ataturk University, Erzurum, Turkey.
SOURCE: Preparative biochemistry & biotechnology, (2002 May) 32 (2) 173-87.
Journal code: 9607037. ISSN: 1082-6068.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20020620
Last Updated on STN: 20021227
Entered Medline: 20021223

L7 ANSWER 2 OF 23 MEDLINE on STN
TI Characteristics of bovine hemoglobin as a potential source of hemoglobin-vesicles for an artificial oxygen carrier.
AB Hemoglobin-vesicles (HbV) have been developed for use as artificial O(2) carriers in which a purified Hb solution is encapsulated within a phospholipid bilayer membrane. In this study, bovine Hb (BHb) was tested as a source of HbV instead of human Hb (HHb). We compared the preparation process and characteristics of BHbV with those of HHbV. The purification of BHb was effectively performed simply with an ultrafiltration system including a process for removing virus and scrapie reagent. The removal ratio of the phospholipid components of bovine red blood cells was over 99.99%, and the **protein** purity was over 99.9%. The deoxygenated and carbonylated BHb showed denaturation transition temperatures at 83 and 87 degrees C, respectively, which are higher than those of HHb (80 and 78 degrees C, respectively), and resistant to pasteurization (**60 degrees** C, 10 h). The purified BHb was concentrated to over 40 g/dl, and encapsulated in a phospholipid bilayer membrane to form BHbV with a diameter of about 280 nm. The O(2) affinity (P(50)) of the BHbV was regulated by coencapsulation of an appropriate amount of Cl(-) (as NaCl), which binds to BHb as an allosteric effector, in the range 16-28 Torr, comparable to human blood (P(50) = 28 Torr). This is quite simple in comparison with HHb which requires phosphate derivatives such as pyridoxal 5'-phosphate as a replacement for 2,3-diphoshoglyceric acid. The viscosity and colloid osmotic pressure of the BHbV when suspended in 5% human serum albumin are 3.5 cP and 20 Torr, respectively, comparable to those of human blood. In conclusion, BHb can be used as a source for the production of HbV, not only because of its abundance in the cattle industry, but also because of the physicochemical advantages of the **purification process**, thermal stability, and regulation

of O(2) affinity in comparison with HHb.
ACCESSION NUMBER: 2002194603 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11927000
TITLE: Characteristics of bovine hemoglobin as a potential source of hemoglobin-vesicles for an artificial oxygen carrier.
AUTHOR: Sakai Hiromi; Masada Yohei; Takeoka Shinji; Tsuchida Eishun
CORPORATE SOURCE: Department of Polymer Chemistry, Advanced Research Institute for Science and Engineering, Waseda University, Tokyo 169-8555, Japan.
SOURCE: Journal of biochemistry, (2002 Apr) 131 (4) 611-7.
Journal code: 0376600. ISSN: 0021-924X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020404
Last Updated on STN: 20021010
Entered Medline: 20021009

L7 ANSWER 3 OF 23 MEDLINE on STN
TI Purification and characterization of a peptidoglycan-associated lipoprotein from Haemophilus influenzae.
AB We have purified to homogeneity a peptidoglycan-associated **protein** from Haemophilus influenzae. Our **purification process** used differential extraction of cell envelopes with nondenaturing detergents. Solubilization of this **protein** was accomplished by heating a peptidoglycan-enriched subcellular fraction in the presence of one of several nondenaturing detergents at 55-**60 degrees** C. The purified **protein** migrated as a single band, with a Mr approximately 15,000, following sodium dodecyl sulfate-polyacrylamide gel electrophoresis. This **protein** contains covalently linked fatty acids, is rich in tyrosine, but lacks methionine and tryptophan. Amino acid analysis also revealed the presence of glycerylcysteine, which has been shown to be the site of fatty acylation in other bacterial lipoproteins. Over 87% of the primary structure has been determined by sequencing high pressure liquid chromatography purified fragments derived from several endoproteinase digests. This **protein** belongs to a family of proteins, known as peptidoglycan associated lipoproteins, which appear to be components of the outer membranes of most Gram-negative bacteria.
ACCESSION NUMBER: 88257108 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3290214
TITLE: Purification and characterization of a peptidoglycan-associated lipoprotein from Haemophilus influenzae.
AUTHOR: Zlotnick G W; Sanfilippo V T; Mattler J A; Kirkley D H; Boykins R A; Seid R C Jr
CORPORATE SOURCE: Department of Protein Chemistry, Praxis Biologics, Inc., Rochester, New York 14623.
SOURCE: Journal of biological chemistry, (1988 Jul 15) 263 (20) 9790-4.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198808
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 20000303
Entered Medline: 19880808

L7 ANSWER 4 OF 23 MEDLINE on STN
TI Purification and partial characterization of human placental particle-bound aminopeptidase.

AB Particle-bound aminopeptidase was purified from the human term placenta by separation of the particles from the soluble fraction by centrifugation and solubilization of the particle fraction with 0.5 per cent (v/v) Triton X-100 followed by CM-cellulose chromatography, Sepharose 6B gel filtration, DE-cellulose and Con A-Sepharose 4B affinity chromatography. Polyacrylamide gel electrophoresis indicated enzymatic and **protein** homogeneity of the purified enzyme. The enzyme seemed to be a glycoprotein with a molecular weight of 320 000. The purified enzyme did not endure freezing but was fairly stable at 4 degrees C. At **60 degrees** C more than half and at 65 degrees C all enzyme activity disappeared in 15 min. The pH dependence of the purified enzyme varied between 6.75 and 7.5, and 6.0 and 6.5, depending on the substrate used. The enzyme hydrolysed most rapidly LeuNA (Km 0.095 +/- 0.008 mmol) followed by beta-naphthylamide derivatives of alanine (Km 0.222 +/- 0.02 mmol), arginine (Km 0.041 +/- 0.002 mmol), lysine (Km 0.084 +/- 0.005 mmol), methionine (Km 0.085 +/- 0.004 mmol) and cystine (Km 0.048 +/- 0.004 mmol). Thus LeuNA was the most specific among the substrates for the enzyme. The **purification process** revealed, however, that CysNA was the most selective substrate for the particulate enzyme, which readily hydrolysed also Leu-p-na (Km 0.865 +/- 0.023 mmol) and Bz-Cys-p-na (Km 0.248 +/- 0.034 mmol).

ACCESSION NUMBER: 83090926 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7178043
TITLE: Purification and partial characterization of human placental particle-bound aminopeptidase.
AUTHOR: Lampelo S; Lalu K; Vanha-Perttula T
SOURCE: Placenta, (1982 Oct-Dec) 3 (4) 379-94.
Journal code: 8006349. ISSN: 0143-4004.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198302
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 20021030
Entered Medline: 19830214

L7 ANSWER 5 OF 23 USPATFULL on STN
TI Phage-associated lytic enzymes for treatment of Bacillus anthracis and related conditions
AB The present disclosure relates to methods, compositions and articles of manufacture useful for the treatment of Bacillus anthracis and B. cereus bacteria and spores, and related conditions. The disclosure further relates to methods and compositions for the identification of a phage associated lytic enzyme to rapidly and specifically detect and kill Bacillus anthracis and other bacteria. Related articles of manufacture, methods of degrading spores and methods of treatment of infections or bacteria populations of, or subjects exposed to or at risk for exposure to, Bacillus anthracis are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2005:4924 USPATFULL
TITLE: Phage-associated lytic enzymes for treatment of Bacillus anthracis and related conditions
INVENTOR(S): Fischetti, Vincent A., West Hempstead, NY, UNITED STATES
Schuch, Raymond, New York, NY, UNITED STATES
Nelson, Daniel, New York, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005004030	A1	20050106
APPLICATION INFO.:	US 2004-849948	A1	20040519 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 2003-US15719, filed

on 19 May 2003, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-380875P	20020517 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO, IL, 60610
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 3071
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 6 OF 23 USPATFULL on STN
TI Long-circulating liposomal compositions
AB A liposome comprising about 1-25 mol % of a phosphatidylglycerol component and about 38-62 mol % of a phosphatidylcholine component is provided herein. In some embodiments, the liposomes further comprise a sterol component, for example a cholesterol.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2005:3896 USPATFULL
TITLE: Long-circulating liposomal compositions
INVENTOR(S): Mehta, Rahul, San Marcos, CA, UNITED STATES
Hardee, Gregory, Rancho Santa Fe, CA, UNITED STATES
Leamon, Christopher P., West Lafayette, IN, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005002999	A1	20050106
APPLICATION INFO.:	US 2004-861983	A1	20040604 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-476037P	20030604 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: COZEN O'CONNOR, P.C., 1900 MARKET STREET, PHILADELPHIA, PA, 19103-3508
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 2541
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 7 OF 23 USPATFULL on STN
TI Chromatographic methods for adenovirus purification
AB This invention provides methods for passing adenovirus particle preparations through chromatographic media to provide purified adenovirus particles.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2004:139011 USPATFULL
TITLE: Chromatographic methods for adenovirus purification
INVENTOR(S): Senesac, Joseph, Houston, TX, UNITED STATES
PATENT ASSIGNEE(S): INTROGEN THERAPEUTICS INC., Austin, TX, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004106184	A1	20040603

APPLICATION INFO.: US 2003-649974 A1 20030827 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-406591P	20020828 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MARSHALL, GERSTEIN & BORUN LLP, 6300 SEARS TOWER, 233 S. WACKER DRIVE, CHICAGO, IL, 60606
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Page(s)
LINE COUNT: 7166
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 8 OF 23 USPATFULL on STN
TI Device and process for the purification of a gaseous effluent
AB The invention concerns a device for purifying a gas effluent containing contaminants, comprising: a reactor including at least an inlet for the gas to be purified and at least an outlet for the purified gas ; at least an ultraviolet or visible radiation source; and at least a support element arranged inside the reactor and coated with a catalyst forming an exposed catalytic surface capable of oxidising at least partly the contaminants under the action of the ultraviolet or visible radiation. The reactor comprises at least two obstructing means, each of said obstructing means obstructing partly the flow of the gas effluent from said inlet up to said outlet and generating a turbulent gas zone on its downstream side, and a catalytic surface is arranged in each turbulent gas zone so that the turbulent gas flow is incident on said catalytic surface.

The invention is applicable to disinfection and pollution management of air and industrial gases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2004:54839 USPATFULL
TITLE: Device and process for the purification of a gaseous effluent
INVENTOR(S): Kartheuser, Benoit, Ciney, BELGIUM
May, Bronislav Henri, Overijse, BELGIUM
Despres, Jean-Francois, Louvain-la-Neuve, BELGIUM

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004040832	A1	20040304
APPLICATION INFO.:	US 2003-463306	A1	20030616 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 2001-EP14742, filed on 13 Dec 2001, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2000-870303	20001215

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: William M. Lee, Jr., Barnes & Thornburg, P.O. Box 2786, Chicago, IL, 60690-2786
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Page(s)
LINE COUNT: 1903
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 9 OF 23 USPATFULL on STN
TI In-situ bonds

AB The invention relates to an organic hydrogel bond for living tissue. The bond is comprised of living tissue pre-treated with hydrogen peroxide, body derived fluids, including at least one NCO-terminated hydrophilic urethane prepolymer, which is derived from an organic polyisocyanate, and oxyethylene-based diols, triols or polyols comprised essentially all of hydroxyl groups capped with polyisocyanate.

ACCESSION NUMBER: 2003:53373 USPATFULL
TITLE: In-situ bonds
INVENTOR(S): Spacek, Paul J., Boston, MA, United States
PATENT ASSIGNEE(S): Praxis, LLC, Mendon, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6524327	B1	20030225
APPLICATION INFO.:	US 2000-676851		20000929 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Izaguirre, Ismael
LEGAL REPRESENTATIVE: Halgren, Don
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 583

L7 ANSWER 10 OF 23 USPATFULL on STN
TI AN IMPROVED METHOD FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS
AB The present invention addresses the need to improve the yields of viral vectors when grown in cell culture systems. In particular, it has been demonstrated that for adenovirus, the use of low-medium perfusion rates in an attached cell culture system provides for improved yields. In other embodiments, the inventors have shown that there is improved Ad-p53 production witrh cells grown in serum-free conditions, and in particular in serum-free suspension culture. Also important to the increase of yields is the use of detergent lysis. Combination of these aspects of the invention permits purification of virus by a single chromatography step that results in purified virus of the same quality as preparations from double CsCl banding using an ultracentrifuge.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2002:322559 USPATFULL
TITLE: AN IMPROVED METHOD FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS
INVENTOR(S): Zhang, Shuyuan, Sugar Land, TX, UNITED STATES
Thwin, Capucine, Spring, TX, UNITED STATES
Wu, Zheng, Sugar Land, TX, UNITED STATES
Cho, Toohyon, UNITED STATES
Gallagher, Shawn, Missouri City, TX, UNITED STATES
PATENT ASSIGNEE(S): Introgen Therapeutics, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002182723	A1	20021205
APPLICATION INFO.:	US 2001-880609	A1	20010612 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-203078, filed on 1 Dec 1998, PENDING Continuation-in-part of Ser. No. US 1997-975519, filed on 20 Nov 1997, GRANTED, Pat. No. US 6194191

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-31329P	19961120 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Steven L. Highlander, FULBRIGHT & JAWORSKI L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX, 78701
NUMBER OF CLAIMS: 43
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 49 Drawing Page(s)
LINE COUNT: 6000
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 11 OF 23 USPATFULL on STN
TI Loading of biologically active solutes into polymer gels
AB Polymer gel networks loaded with biologically active solutes in a manner that solute activity is maintained and protected from thermal and/or chemical degradation while in the gel network are provided. The invention also provides for effects of modulating parameters for loading safe responsive gel networks using loading solutions containing phase separating polymers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1998:147065 USPATFULL
TITLE: Loading of biologically active solutes into polymer gels
INVENTOR(S): Roos, Eric J., 1 Barbara Jean St., Grafton, MA, United States 01519
Schiller, Matthew E., 23C Sagamore Way, Waltham, MA, United States 02154

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5840338		19981124
APPLICATION INFO.:	US 1995-556130		19951106 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-276462, filed on 18 Jul 1994, now patented, Pat. No. US 5603955 And a continuation-in-part of Ser. No. US 1994-276193, filed on 18 Jul 1994
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Webman, Edward J.
LEGAL REPRESENTATIVE: Choate, Hall& Stewart
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 25 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 4589
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 12 OF 23 USPATFULL on STN
TI Enhanced loading of solutes into polymer gels and methods of use
AB A method of loading a drug into a crosslinked polymer network and protecting the drug from the effects of inactivation is described. The method includes the steps of contacting a biologically active solute (e.g. drug) with: (i) a gel network; (ii) a loading polymer that is somewhat immiscible with the gel; and (iii) a salt, under conditions sufficient for the biologically active solute to selectively partition into the gel and the salt and the loading polymer to be entrained in the gel. A drug delivery system including a polymer gel network and the drug to be delivered is also described. The system also includes a salt and/or a loading polymer. The system protects the drug from loss of activity. In one embodiment, the polymer gel network is capable of expanding or collapsing in response to a change in an environmental condition to which the gel is exposed, the expanding or collapsing sufficient to release the drug into an environment of use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 97:91191 USPATFULL
TITLE: Enhanced loading of solutes into polymer gels and methods of use
INVENTOR(S): Gehrke, Steven Henry, Cincinnati, OH, United States
Lupton, E. C., Boston, MA, United States
Schiller, Matthew E., Waltham, MA, United States
Uhden, Lorelle, Cincinnati, OH, United States
Vaid, Nitin, Kanpur, India
PATENT ASSIGNEE(S): University of Cincinnati, Cincinnati, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5674521		19971007
APPLICATION INFO.:	US 1995-425275		19950420 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-276462, filed on 18 Jul 1994, now patented, Pat. No. US 5603955
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Azpuru, Carlos A.
LEGAL REPRESENTATIVE: Choate, Hall & Stewart
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 1966
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 13 OF 23 USPATFULL on STN
TI 11,7 Substituted camptothecin derivatives and formulations of 11,7 substituted camptothecin derivatives and methods for uses thereof
AB The novel compounds 11-hydroxy-7-ethyl camptothecin and 11-hydroxy-7-methoxy camptothecin (11,7-HECPT and 11,7-HMCPT) are active anticancer compounds which are poorly soluble in water. Because of their novelty, 11,7-HECPT and 11,7-HMCPT derivatives have not been directly administered by parenteral or oral routes to human subjects as an antitumor composition for the purpose of inhibiting the growth of cancer cells. The claimed compositions are useful as compared to the water soluble camptothecin derivatives, such as CPT-11, in clinical trials. The unpredictable interpatient variability in the metabolic production of an active metabolite from CPT-11 limits the utility of CPT-11. This invention overcomes these limitations by claiming novel pharmaceutically acceptable lactone stable formulations of 11,7-HECPT or 11,7-HMCPT, to directly administer to patients. The present invention also claims 11,7-HECPT and 11,7-HMCPT compositions, the synthesis of 11,7-HECPT or 11,7-HMCPT, the methods of formulation of 11,7-HECPT or 11,7 -HMCPT, and the methods of use of 11,7-HECPT or 11,7-HMCPT. Additionally, the claimed invention is directed to novel dosages, schedules, and routes of administration for both the 11,7-HECPT or 11,7-HMCPT formulations to humans with various forms of cancer. Other embodiments of this invention include isolation methods and methods of synthesis of certain camptothecin derivatives.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 97:45023 USPATFULL
TITLE: 11,7 Substituted camptothecin derivatives and formulations of 11,7 substituted camptothecin derivatives and methods for uses thereof
INVENTOR(S): Hausheer, Frederick H., San Antonio, TX, United States
Haridas, Kochat, Houston, TX, United States
PATENT ASSIGNEE(S): BioNumerik Pharmaceuticals, Inc., San Antonio, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE

PATENT INFORMATION: US 5633260 19970527
APPLICATION INFO.: US 1995-518644 19950824 (8)
RELATED APPLN. INFO.: Division of Ser. No. US 1994-229527, filed on 19 Apr 1994, now patented, Pat. No. US 5468754
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Dodd, Thomas J.
NUMBER OF CLAIMS: 42
EXEMPLARY CLAIM: 1
LINE COUNT: 2223
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 14 OF 23 USPATFULL on STN
TI Enhanced loading of solutes into polymer gels
AB A method of loading a drug into a crosslinked polymer network and protecting the drug from the effects of inactivation is described. The method includes the steps of contacting of a biologically active solute (i.e., drug) with:(i) a gel network; (ii) a second protectant polymer that is somewhat immiscible with the gel; and (iii) a protectant salt, under conditions sufficient for the biologically active solute to selectively partition into the gel and the protectants to be entrained in the gel. Most preferably, the gel network is a crosslinked gel responsive to a change in an environmental condition to which the gel is exposed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 97:14434 USPATFULL
TITLE: Enhanced loading of solutes into polymer gels
INVENTOR(S): Gehrke, Stevin H., Cincinnati, OH, United States
Lupton, E. C., Boston, MA, United States
Schiller, Matthew E., Waltham, MA, United States
Uhden, Lorelle, Cincinnati, OH, United States
Vaid, Nitin, Kanpur, India
PATENT ASSIGNEE(S): University of Cincinnati, Cincinnati, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5603955		19970218
APPLICATION INFO.:	US 1994-276462		19940718 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Webman, Edward J.
LEGAL REPRESENTATIVE: Choate, Hall & Stewart
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 1934
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 15 OF 23 USPATFULL on STN
TI Process and product for treatment of rheumatoid arthritis
AB This invention provides a therapeutic pill comprising animal tissue containing a therapeutic amount of Type II collagen and a method of preparing animal tissue containing Type II collagen for treatment of Rheumatoid Arthritis in humans.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 96:55544 USPATFULL
TITLE: Process and product for treatment of rheumatoid arthritis
INVENTOR(S): Moore, Eugene R., 5600 Woodview Pass, Midland, MI, United States 48642

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5529786		19960625	
APPLICATION INFO.:	US 1994-202723		19940228	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Spear, James M.
LEGAL REPRESENTATIVE: Davey, Merlin B.
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
LINE COUNT: 394
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 16 OF 23 USPATFULL on STN
TI Therapeutic grade thrombin produced by chromatography
AB A process for the large-scale production of therapeutic grade thrombin of excellent viral safety and storage-stability is carried out by purification of viricide treated crude thrombin by ion-exchange chromatography on a single column using a sulfalkyl-activated polysaccharide, particularly a non-compressible composite medium of sulfoalkyl-activated dextran and silica particles, as the ion exchange medium and using increasing concentrations of phosphate buffer for elution. After recovery of thrombin in the final eluate, the phosphate buffer is exchanged for a stabilizing formulation buffer, and the stabilized thrombin is subjected to viral filtration and optional dry heat treatment for further viral inactivation. The final product has high specific activity and is obtained in good yield.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 96:29457 USPATFULL
TITLE: Therapeutic grade thrombin produced by chromatography
INVENTOR(S): Proba, Zbigniew, 3067 Murray Avenue, Chomedey, Laval, Quebec, Canada
Brodniewicz, Teresa, 3067 Murray Avenue, Chomedey, Laval, Quebec, Canada H7V 2H2

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5506127		19960409	
APPLICATION INFO.:	US 1994-309583		19940921	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Naff, David M.
ASSISTANT EXAMINER: Meller, Michael V.
LEGAL REPRESENTATIVE: Hoffman, Wasson & Gitler
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 601
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 17 OF 23 USPATFULL on STN
TI 11,7 substituted camptothecin derivatives and formulations of 11,7 substituted camptothecin derivatives and methods for uses thereof
AB The novel compounds 11-hydroxy-7-ethyl camptothecin and 11-hydroxy-7-methoxy camptothecin (11,7-HECPT and 11,7-HMCPT) are active anticancer compounds which are poorly soluble in water. Because of their novelty, 11,7-HECPT and 11,7-HMCPT derivatives have not been directly administered by parenteral or oral routes to human subjects as an antitumor composition for the purpose of inhibiting the growth of cancer cells. The claimed compositions are useful as compared to the water soluble camptothecin derivatives, such as CPT-11, in clinical trials. The unpredictable interpatient variability in the metabolic production

of an active metabolite from CPT-11 limits the utility of CPT-11. This invention overcomes these limitations by claiming novel pharmaceutically acceptable lactone stable formulations of 11,7-HECPT or 11,7-HMCPT, to directly administer to patients. The present invention also claims 11,7-HECPT and 11,7-HMCPT compositions, the synthesis of 11,7-HECPT or 11,7-HMCPT, the methods of formulation of 11,7-HECPT or 11,7-HMCPT, and the methods of use of 11,7-HECPT or 11,7-HMCPT. Additionally, the claimed invention is directed to novel dosages, schedules, and routes of administration for both the 11,7-HECPT or 11,7-HMCPT formulations to humans with various forms of cancer. Other embodiments of this invention include isolation methods and methods of synthesis of certain camptothecin derivatives.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	95:103516 USPATFULL		
TITLE:	11,7 substituted camptothecin derivatives and formulations of 11,7 substituted camptothecin derivatives and methods for uses thereof		
INVENTOR(S):	Hausheer, Frederick H., San Antonio, TX, United States Haridas, Kochat, Houston, TX, United States		
PATENT ASSIGNEE(S):	BioNumerik Pharmaceuticals, Inc., San Antonio, TX, United States (U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5468754		19951121
APPLICATION INFO.:	US 1994-229527		19940419 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Daus, Donald G.		
LEGAL REPRESENTATIVE:	Fish & Richardson		
NUMBER OF CLAIMS:	36		
EXEMPLARY CLAIM:	1		
LINE COUNT:	2348		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 18 OF 23 USPATFULL on STN

TI Diamine oxidase and assay for rupture of amniotic membrane in pregnant mammals

AB Assay for detection of a form of diamine oxidase which is present only in amniotic fluid and, more especially, for detection of amniotic membrane rupture by detection of the amniotic fluid diamine oxidase. The assay includes the steps of detecting the amniotic fluid diamine oxidase and distinguishing that from another form of diamine oxidase found in serum. The assay may be carried out on a sample of vaginal fluid from a pregnant female wherein the sample is subjected to the assay to detect the leakage or presence of amniotic fluid diamine oxidase. Purified forms of amniotic fluid diamine oxidase and serum diamine oxidase which is different from amniotic fluid diamine oxidase and found in serum are also described, together with a method of purifying both forms of diamine oxidase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	94:11319 USPATFULL		
TITLE:	Diamine oxidase and assay for rupture of amniotic membrane in pregnant mammals		
INVENTOR(S):	Cowley, David M., Brisbane, Australia Maguire, David J., Brisbane, Australia Voroteliak, Victor, Brisbane, Australia		
PATENT ASSIGNEE(S):	Griffith University, Queensland, Australia (non-U.S. corporation)		
	NUMBER	KIND	DATE

PATENT INFORMATION: US 5284749 19940208
APPLICATION INFO.: US 1990-623168 19901031 (7)
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Yarbrough, Amelia Burgess
ASSISTANT EXAMINER: Yuan, Lori L.
LEGAL REPRESENTATIVE: Nixon & Vanderhye
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 6
NUMBER OF DRAWINGS: 14 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 1266
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 19 OF 23 USPATFULL on STN
TI Electrodeposited foil with controlled properties for printed circuit board applications and procedures and electrolyte bath solutions for preparing the same
AB Copper conductive foil for use in preparing printed circuit boards is electrodeposited from an electrolyte solution containing copper ions, sulphate ions, animal glue and thiourea. The thiourea operates to decrease the roughness of the foil, to enable operation at higher current densities and/or to modify the ductility characteristics of the foil.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 93:43885 USPATFULL
TITLE: Electrodeposited foil with controlled properties for printed circuit board applications and procedures and electrolyte bath solutions for preparing the same
INVENTOR(S): DiFranco, Dino F., Mayfield Village, OH, United States
Clouser, Sidney J., Chardon, OH, United States
PATENT ASSIGNEE(S): Gould Inc., Eastlake, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5215645		19930601	
APPLICATION INFO.:	US 1989-406894		19890913	(7)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Tufariello, T. M.
LEGAL REPRESENTATIVE: Renner, Otto, Boisselle & Sklar
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1052
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 20 OF 23 USPATFULL on STN
TI Purified Bacillus licheniformis PWD-1 keratinase
AB A substantially pure keratinaceous material-degrading B. licheniformis PWD-1 enzyme is disclosed. The substantially pure enzyme is characterized by a molecular weight of 33 kiloDaltons, an isoelectric point of 7.25, an optimum pH of 7.5, an optimum temperature of 45°-50° C., and thermal stability at low temperatures.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 92:102998 USPATFULL
TITLE: Purified Bacillus licheniformis PWD-1 keratinase
INVENTOR(S): Shih, Jason C. H., Cary, NC, United States
Williams, C. Michael, Cary, NC, United States
PATENT ASSIGNEE(S): North Carolina State University, Raleigh, NC, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5171682		19921215
APPLICATION INFO.:	US 1991-769553		19911001 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1990-581681, filed on 13 Sep 1990, now patented, Pat. No. US 5063161 which is a continuation of Ser. No. US 1988-175476, filed on 31 Mar 1988, now patented, Pat. No. US 4959311, issued on 25 Sep 1990
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wax, Robert A.
ASSISTANT EXAMINER: Hendricks, Keith D.
LEGAL REPRESENTATIVE: Bell, Seltzer, Park & Gibson
NUMBER OF CLAIMS: 1
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 758
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 21 OF 23 USPATFULL on STN
TI Copper foils for printed circuit board applications and procedures and electrolyte bath solutions for electrodepositing the same
AB Copper conductive foil for use in preparing printed circuit boards is electrodeposited from an electrolyte solution containing copper ions, sulphate ions and thiourea. The thiourea operates to decrease the roughness of the foil, to enable operation at higher current densities, and/or to modify the tensile strength and ductility characteristics of the foil. An IPC Class 2 foil is prepared without annealing.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 92:102735 USPATFULL
TITLE: Copper foils for printed circuit board applications and procedures and electrolyte bath solutions for electrodepositing the same
INVENTOR(S): DiFranco, Dino F., Mayfield Village, OH, United States
Clouser, Sidney J., Chardon, OH, United States
PATENT ASSIGNEE(S): Gould Inc., Eastlake, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5171417		19921215
APPLICATION INFO.:	US 1990-510231		19900418 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1989-406894, filed on 13 Sep 1989
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Tufariello, T. M.
LEGAL REPRESENTATIVE: Renner, Otto, Boisselle & Sklar
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1069
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 22 OF 23 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI A palladium complex-promoted hydrolytic polypeptide cleavage process for cleaving the polypeptide at a Cys-His cleavage site, comprises solubilizing the polypeptide in mixture of a palladium promotor dissolved in organic acid solvent.
AN 2004-053266 [05] WPIDS
AB WO2003100015 A UPAB: 20040120
NOVELTY - A palladium complex-promoted hydrolytic polypeptide cleavage

process, which selectively cleaves the polypeptide at a Cys-His cleavage site, comprises solubilizing the polypeptide in a reaction mixture comprised of a palladium promotor dissolved in a high-concentration organic acid solvent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) A peptide **purification process**; and
(2) A process for producing a peptide.

USE - The methods are useful for selectively cleaving the polypeptide at Cys-His cleavage site (claimed).

ADVANTAGE - The process provides a highly specific, conformationally independent, palladium promoted hydrolytic cleavage of polypeptides, including cleavage of relatively insoluble chimeric proteins in the form of inclusion bodies.

Dwg.0/10

ACCESSION NUMBER: 2004-053266 [05] WPIDS
DOC. NO. CPI: C2004-021423
TITLE: A palladium complex-promoted hydrolytic polypeptide cleavage process for cleaving the polypeptide at a Cys-His cleavage site, comprises solubilizing the polypeptide in mixture of a palladium promotor dissolved in organic acid solvent.
DERWENT CLASS: B04 D16
INVENTOR(S): HOLMQUIST, B; SEO, J S; STRYDOM, D
PATENT ASSIGNEE(S): (REST-N) RESTORAGEN INC
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003100015	A2	20031204	(200405)*	EN	46

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003237244	A1	20031212	(200443)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003100015	A2	WO 2003-US16468	20030523
AU 2003237244	A1	AU 2003-237244	20030523

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003237244	A1	Based on	WO 2003100015

PRIORITY APPLN. INFO: US 2002-383488P 20020524

L7 ANSWER 23 OF 23 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
TI A palladium complex-promoted hydrolytic polypeptide cleavage process for cleaving the polypeptide at a Cys-His cleavage site, comprises solubilizing the polypeptide in mixture of a palladium promotor dissolved in organic acid solvent.
AN 2004-053266 [05] WPIX
AB WO2003100015 A UPAB: 20040120
NOVELTY - A palladium complex-promoted hydrolytic polypeptide cleavage process, which selectively cleaves the polypeptide at a Cys-His cleavage site, comprises solubilizing the polypeptide in a reaction mixture

comprised of a palladium promotor dissolved in a high-concentration organic acid solvent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) A peptide **purification process**; and
(2) A process for producing a peptide.

USE - The methods are useful for selectively cleaving the polypeptide at Cys-His cleavage site (claimed).

ADVANTAGE - The process provides a highly specific, conformationally independent, palladium promoted hydrolytic cleavage of polypeptides, including cleavage of relatively insoluble chimeric proteins in the form of inclusion bodies.

Dwg.0/10

ACCESSION NUMBER: 2004-053266 [05] WPIX
DOC. NO. CPI: C2004-021423
TITLE: A palladium complex-promoted hydrolytic polypeptide cleavage process for cleaving the polypeptide at a Cys-His cleavage site, comprises solubilizing the polypeptide in mixture of a palladium promotor dissolved in organic acid solvent.
DERWENT CLASS: B04 D16
INVENTOR(S): HOLMQUIST, B; SEO, J S; STRYDOM, D
PATENT ASSIGNEE(S): (REST-N) RESTORAGEN INC
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003100015	A2	20031204	(200405)*	EN	46
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003237244	A1	20031212	(200443)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003100015	A2	WO 2003-US16468	20030523
AU 2003237244	A1	AU 2003-237244	20030523

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003237244	A1 Based on	WO 2003100015

PRIORITY APPLN. INFO: US 2002-383488P 20020524

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(FILE 'HOME' ENTERED AT 12:27:15 ON 02 MAR 2005)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS, JAPIO, WPIX, BIOTECHDS, BIOSIS, BIOBUSINESS' ENTERED AT 12:27:55 ON 02 MAR 2005

L1 0 S PURIFICATION PROCEES AND (FERMENTATION PRODUCT) AND (TEMPERAT
L2 87 S PURIFICATION PROCESS AND (60 DEGREES)
L3 0 S L2 AND (60 DEGREES TO 90 DEGREES)
L4 7 S L2 AND (COOLING TO 59 DEGREES OR 58 DEGREES OR 57 DEGREES OR
L5 5656 S PURIFICATION PROCESS AND (HEATING OR COOLING)

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L6            60 S L5 AND (59 DEGREES OR 60 DEGREES)
L7            23 S L2 AND PROTEIN

=> s l6 and fermentation broth
L8             0 L6 AND FERMENTATION BROTH

=> s GLP-1
   5 FILES SEARCHED...
L9         12665 GLP-1

=> s exendin-4 or exendin-3
   9 FILES SEARCHED...
L10         1773 EXENDIN-4 OR EXENDIN-3

=> s l10 and l5
L11            2 L10 AND L5

=> d l11 ti abs ibib tot

L11  ANSWER 1 OF 2  USPATFULL on STN
TI     Purification process comprising microfiltration at
       elevated temperatures
AB     Process for microfiltration at elevated temperature.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER:         2004:212922  USPATFULL
TITLE:                    Purification process comprising
                          microfiltration at elevated temperatures
INVENTOR(S):              Christensen, Lars Hojlund, Vaerlose, DENMARK
                          Nielsen, Torben Kjaersgaard, Roskilde, DENMARK

                               NUMBER        KIND    DATE
                          ---------------- ------ --------
PATENT INFORMATION:       US 2004164023      A1   20040826
APPLICATION INFO.:        US 2003-671064     A1   20030925  (10)

                                 NUMBER         DATE
                          ------------------ --------
PRIORITY INFORMATION:     DK 2002-1422       20020925
                          US 2002-413729P    20020926 (60)
DOCUMENT TYPE:            Utility
FILE SEGMENT:             APPLICATION
LEGAL REPRESENTATIVE:     NOVO NORDISK PHARMACEUTICALS, INC, 100 COLLEGE ROAD
                          WEST, PRINCETON, NY, 08540
NUMBER OF CLAIMS:         34
EXEMPLARY CLAIM:          1
NUMBER OF DRAWINGS:       2 Drawing Page(s)
LINE COUNT:               629
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11  ANSWER 2 OF 2  USPATFULL on STN
TI     Secondary binding site of dipeptidyl peptidase IV (DP IV)
AB     The present application relates to the secondary binding site of
       dipeptidyl peptidase IV, its relationship amongst substrates and to the
       modulation of substrate specificity of dipeptidyl peptidase IV (DP IV,
       synonym: DPP IV, CD26, EC 3.4.14.5). The application relates further to
       compounds that bind to the secondary binding site of DP IV and their use
       to modulate the substrate specificity of DP IV; methods of treatment of
       various DP IV mediated disorders; and screening methods for the
       identification of secondary binding sites on DP IV and DP IV-like
       enzymes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER:         2004:77097  USPATFULL
```

TITLE: Secondary binding site of dipeptidyl peptidase IV (DP IV)
INVENTOR(S): Hoffmann, Torsten, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Kuehn-Wache, Kerstin, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Demuth, Hans-Ulrich, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Brandt, Wolfgang, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Baer, Jochaim, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004058876	A1	20040325	
APPLICATION INFO.:	US 2002-246817	A1	20020918	(10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BROWN, RUDNICK, BERLACK & ISRAELS, LLP., BOX IP, 18TH FLOOR, ONE FINANCIAL CENTER, BOSTON, MA, 02111
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 22 Drawing Page(s)
LINE COUNT: 2415
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 12:27:15 ON 02 MAR 2005)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS, JAPIO, WPIX, BIOTECHDS, BIOSIS, BIOBUSINESS' ENTERED AT 12:27:55 ON 02 MAR 2005

L1	0	S	PURIFICATION PROCEES AND (FERMENTATION PRODUCT) AND (TEMPERAT
L2	87	S	PURIFICATION PROCESS AND (60 DEGREES)
L3	0	S	L2 AND (60 DEGREES TO 90 DEGREES)
L4	7	S	L2 AND (COOLING TO 59 DEGREES OR 58 DEGREES OR 57 DEGREES OR
L5	5656	S	PURIFICATION PROCESS AND (HEATING OR COOLING)
L6	60	S	L5 AND (59 DEGREES OR 60 DEGREES)
L7	23	S	L2 AND PROTEIN
L8	0	S	L6 AND FERMENTATION BROTH
L9	12665	S	GLP-1
L10	1773	S	EXENDIN-4 OR EXENDIN-3
L11	2	S	L10 AND L5

=> s l4 and human serum albumin
3 FILES SEARCHED...
L12 0 L4 AND HUMAN SERUM ALBUMIN

=> s l9 and l5
L13 4 L9 AND L5

=> d l13 ti abs ibib tot

L13 ANSWER 1 OF 4 USPATFULL on STN
TI **Purification process** comprising microfiltration at elevated temperatures
AB Process for microfiltration at elevated temperature.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2004:212922 USPATFULL
TITLE: **Purification process** comprising microfiltration at elevated temperatures

INVENTOR(S): Christensen, Lars Hojlund, Vaerlose, DENMARK
Nielsen, Torben Kjaersgaard, Roskilde, DENMARK

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004164023	A1	20040826
APPLICATION INFO.:	US 2003-671064	A1	20030925 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	DK 2002-1422	20020925
	US 2002-413729P	20020926 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: NOVO NORDISK PHARMACEUTICALS, INC, 100 COLLEGE ROAD WEST, PRINCETON, NY, 08540
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 629
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 2 OF 4 USPATFULL on STN
TI Chromatographic methods for adenovirus purification
AB This invention provides methods for passing adenovirus particle preparations through chromatographic media to provide purified adenovirus particles.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2004:139011 USPATFULL
TITLE: Chromatographic methods for adenovirus purification
INVENTOR(S): Senesac, Joseph, Houston, TX, UNITED STATES
PATENT ASSIGNEE(S): INTROGEN THERAPEUTICS INC., Austin, TX, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004106184	A1	20040603
APPLICATION INFO.:	US 2003-649974	A1	20030827 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-406591P	20020828 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MARSHALL, GERSTEIN & BORUN LLP, 6300 SEARS TOWER, 233 S. WACKER DRIVE, CHICAGO, IL, 60606
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Page(s)
LINE COUNT: 7166
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 3 OF 4 USPATFULL on STN
TI Secondary binding site of dipeptidyl peptidase IV (DP IV)
AB The present application relates to the secondary binding site of dipeptidyl peptidase IV, its relationship amongst substrates and to the modulation of substrate specificity of dipeptidyl peptidase IV (DP IV, synonym: DPP IV, CD26, EC 3.4.14.5). The application relates further to compounds that bind to the secondary binding site of DP IV and their use to modulate the substrate specificity of DP IV; methods of treatment of various DP IV mediated disorders; and screening methods for the identification of secondary binding sites on DP IV and DP IV-like enzymes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2004:77097 USPATFULL
TITLE: Secondary binding site of dipeptidyl peptidase IV (DP IV)
INVENTOR(S): Hoffmann, Torsten, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Kuehn-Wache, Kerstin, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Demuth, Hans-Ulrich, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Brandt, Wolfgang, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Baer, Jochaim, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004058876	A1	20040325	
APPLICATION INFO.:	US 2002-246817	A1	20020918	(10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BROWN, RUDNICK, BERLACK & ISRAELS, LLP., BOX IP, 18TH FLOOR, ONE FINANCIAL CENTER, BOSTON, MA, 02111
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 22 Drawing Page(s)
LINE COUNT: 2415
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 4 OF 4 USPATFULL on STN
TI AN IMPROVED METHOD FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS
AB The present invention addresses the need to improve the yields of viral vectors when grown in cell culture systems. In particular, it has been demonstrated that for adenovirus, the use of low-medium perfusion rates in an attached cell culture system provides for improved yields. In other embodiments, the inventors have shown that there is improved Ad-p53 production witrh cells grown in serum-free conditions, and in particular in serum-free suspension culture. Also important to the increase of yields is the use of detergent lysis. Combination of these aspects of the invention permits purification of virus by a single chromatography step that results in purified virus of the same quality as preparations from double CsCl banding using an ultracentrifuge.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2002:322559 USPATFULL
TITLE: AN IMPROVED METHOD FOR THE PRODUCTION AND PURIFICATION OF ADENOVIRAL VECTORS
INVENTOR(S): Zhang, Shuyuan, Sugar Land, TX, UNITED STATES
Thwin, Capucine, Spring, TX, UNITED STATES
Wu, Zheng, Sugar Land, TX, UNITED STATES
Cho, Toohyon, UNITED STATES
Gallagher, Shawn, Missouri City, TX, UNITED STATES
PATENT ASSIGNEE(S): Introgen Therapeutics, Inc. (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002182723	A1	20021205	
APPLICATION INFO.:	US 2001-880609	A1	20010612	(9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-203078, filed on 1 Dec 1998, PENDING Continuation-in-part of Ser. No. US 1997-975519, filed on 20 Nov 1997, GRANTED, Pat. No. US 6194191

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-31329P	19961120 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Steven L. Highlander, FULBRIGHT & JAWORSKI L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX, 78701
NUMBER OF CLAIMS: 43
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 49 Drawing Page(s)
LINE COUNT: 6000
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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=> e markussen, j/au
E1            6     MARKUSSEN T/AU
E2            1     MARKUSSEN TORSTEN/AU
E3            0 --> MARKUSSEN, J/AU
E4           30     MARKUSSIS V/AU
E5            5     MARKUSSIS VIRON/AU
E6            1     MARKUSSON/AU
E7            4     MARKUSSON A/AU
E8            1     MARKUSSON ANITA/AU
E9            8     MARKUSSON D/AU
E10           2     MARKUSSON DAN/AU
E11           1     MARKUSSON E/AU
E12           1     MARKUSSON EYSTEIN/AU

=> e diers, i/au
E1            6     DIERS W F/AU
E2            1     DIERS WILFRED F/AU
E3            0 --> DIERS, I/AU
E4            1     DIERSBOCK GUNTHER RUDALPH/AU
E5            4     DIERSBOCK GUNTHER RUDOLPH/AU
E6            4     DIERSCH/AU
E7            2     DIERSCH H/AU
E8            6     DIERSCH H J/AU
E9            2     DIERSCH HANS JOERG/AU
E10          25     DIERSCH R/AU
E11           2     DIERSCH REGINE/AU
E12           9     DIERSCH RUDOLF/AU
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NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
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NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 13:07:58 ON 02 MAR 2005

=> file medline
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 13:08:30 ON 02 MAR 2005

 FILE LAST UPDATED: 1 MAR 2005 (20050301/UP).  FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available.  For details enter HELP
 RLOAD at an arrow promt (=>).  See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2005 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s purification process
        547103 PURIFICATION
        380846 PROCESS
L1         549 PURIFICATION PROCESS
               (PURIFICATION(W)PROCESS)

=> s l1 and (heating and cooling steps)
         19691 HEATING
         13883 COOLING
         63432 STEPS
            12 COOLING STEPS
               (COOLING(W)STEPS)
L2           0 L1 AND (HEATING AND COOLING STEPS)

=> s l1 and (heating)
         19691 HEATING
L3           6 L1 AND (HEATING)

=> s l3 and cooling
         13883 COOLING
L4           0 L3 AND COOLING

=> s l1 and cooling
         13883 COOLING
L5           1 L1 AND COOLING

=> d l5 ti abs ibib tot

L5   ANSWER 1 OF 1     MEDLINE on STN
TI   Comparison of purification procedures for the isolation and detection of
     anabolic residues in faeces using gas chromatography-mass spectrometry.
```

AB Within several regional field laboratories and the national reference laboratory a harmonised methodology for the analysis of anabolic residues in faecal samples was developed. The method consists of a liquid-liquid and a solid-phase extraction step, followed by a high-performance liquid chromatography purification step. Using gas chromatography-mass spectrometry, currently illegally used anabolic steroids can be detected in faeces at the ppb level. Within this context acidification, followed by centrifugation under **cooling**, allows efficient, practical and rapid defatting of faecal samples. Furthermore, a combination of a silica and an aminopropyl solid-phase extraction column was found to give the best results as regards the sample **purification process**

ACCESSION NUMBER: 1999364169 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10435311
TITLE: Comparison of purification procedures for the isolation and detection of anabolic residues in faeces using gas chromatography-mass spectrometry.
AUTHOR: Hamoir T; Courtheyn D; De Brabander H; Delahaut P; Leyssens L; Pottie G
CORPORATE SOURCE: Institute of Public Health, Brussels, Belgium.
SOURCE: Analyst, (1998 Dec) 123 (12) 2621-4.
Journal code: 0372652. ISSN: 0003-2654.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990909

=> d his

(FILE 'HOME' ENTERED AT 13:07:58 ON 02 MAR 2005)

FILE 'MEDLINE' ENTERED AT 13:08:30 ON 02 MAR 2005
L1 549 S PURIFICATION PROCESS
L2 0 S L1 AND (HEATING AND COOLING STEPS)
L3 6 S L1 AND (HEATING)
L4 0 S L3 AND COOLING
L5 1 S L1 AND COOLING

=> d l6 ti abs ibib tot
L6 NOT FOUND
The L-number entered has not been defined in this session, or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> d l3 ti abs ibib tot

L3 ANSWER 1 OF 6 MEDLINE on STN
TI The safety of fibrin sealants.
AB Fibrin sealants are prepared from fibrinogen, thrombin and sometimes also factor XIII that have been purified from human plasma. Bovine aprotinin is also included in some preparations. Each of these components has the potential to carry blood-borne pathogens, albeit at a very low frequency. In order to minimize the risk of viral transmission from commercial fibrin sealants, plasma donations undergo a series of procedures that contribute to avoiding, inactivating and eliminating potential contaminants. The procedures for selection and screening of plasma donors, and the testing of donated plasma, incorporates highly sensitive molecular techniques (e.g. PCR testing) and contributes significantly to reducing the theoretical possibility of viral transmission. The starting material for

bovine aprotinin is also carefully selected, and the manufacturing process rigorously assessed, to minimize the putative risk of transmission of bovine spongiform encephalopathies. The manufacturing process for commercial fibrin sealants comprises a range of procedures, including heat treatment (e.g. pasteurization, dry or vapor **heating**), filtration, solvent/detergent treatment, precipitation, pH treatment and chromatography. Some steps are an inherent part of the **purification process** and others (e.g. pasteurization, nanofiltration) are deliberately introduced to inactivate/eliminate potential pathogens. Current manufacturing processes provide a very high degree of safety for fibrin sealants. In 20 years of worldwide use, there have been no known cases of hepatitis or HIV transmission associated with the use of commercial fibrin sealants.

ACCESSION NUMBER: 2003337011 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12869985
TITLE: The safety of fibrin sealants.
AUTHOR: Joch Christine
CORPORATE SOURCE: Global Drug Surveillance, Aventis Behring GmbH, PO Box 1230, D-35002 Marburg, Germany.. christine.joch@aventis.com
SOURCE: Cardiovascular surgery (London, England), (2003 Aug) 11 Suppl 1 23-8.
Journal code: 9308765. ISSN: 0967-2109.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20030719
Last Updated on STN: 20031218
Entered Medline: 20031120

L3 ANSWER 2 OF 6 MEDLINE on STN
TI Strategies to avoid virus transmissions by biopharmaceutic products.
AB The use of biopharmaceutical products offers an opportunity for the treatment of many diseases. Biotechnical manufacturing using recombinant mammalian cell lines is the most appropriate method today for the production of biopharmaceutical protein drugs for the treatment of human and animal diseases. However, mammalian cell line derived products have a potential risk for virus transmission to patients who are treated with these biopharmaceutical products. The reliability that biological products are free of any viruses requires a combination of several strategies: The use of well-characterized cell bank systems and, if feasible, the avoidance of biological raw materials for the cultivation of these mammalian cell lines and the production of biopharmaceuticals. Further on, the **purification process** for biopharmaceuticals has to be validated for its ability to efficiently remove and inactivate any potential virus contamination and, where applicable, also unconventional transmissible agents, such as BSE. In addition, the biopharmaceutical product itself can be tested for the presence of viruses. Like other manufacturing processes, biotechnical production processes have to be performed in compliance with current Good Manufacturing Practices (cGMP).

ACCESSION NUMBER: 1998075464 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9413543
TITLE: Strategies to avoid virus transmissions by biopharmaceutic products.
AUTHOR: Werz W; Hoffmann H; Haberer K; Walter J K
CORPORATE SOURCE: Dr. Karl Thomae GmbH, Boehringer Ingelheim, Department of Biotech Production, Biberach/Riss, Federal Republic of Germany.
SOURCE: Archives of virology. Supplementum, (1997) 13 245-56.
Journal code: 9214275. ISSN: 0939-1983.
PUB. COUNTRY: Austria
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980126

L3 ANSWER 3 OF 6 MEDLINE on STN
TI Production, purification and characterization of Bacillus lipase.
AB The lipolytic activities in the supernatant fractions of Bacillus cereus and Bacillus coagulans cultures were investigated. Aeration, agitation, different media, emulsified oils, inoculum size and phase of growth affected lipase production. Aeration was essential for lipase production (air: medium ration 4:1) and produced the highest activity. The lipolytic activity reached a maximum level after incubation for two days with continuous agitation. It was also elevated by the presence of either olive oil or tributyrin and with lesser extent in the presence of castor oil. The enzyme levels were drastically reduced in the presence of animal fat, cotton seed oil, margarine or glycerol. The extracellular lipase enzyme from Bacillus cereus was purified with 46.2% overall recovery thought too steps, an acetone precipitation of the whole supernatant and purification by gel filtration on sephadex G-100. The efficiency of the **purification process** was evaluated through the polyacrylamide gel electrophoresis. The enzyme has an optimum pH 7.5 at the optimum incubation temperature of 40 degrees C. It is stable and retains its full activity after **heating** at 40-50 degrees C for 30 min. The activity is lost completely at 80 degrees C.
ACCESSION NUMBER: 97410479 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9265771
TITLE: Production, purification and characterization of Bacillus lipase.
AUTHOR: el-Shafei H A; Rezkallah L A
CORPORATE SOURCE: Microbial Chemistry Department, National Research Centre, Dokki, Cairo, Egypt.
SOURCE: Microbiological research, (1997 Jul) 152 (2) 199-208. Journal code: 9437794. ISSN: 0944-5013.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971024
Last Updated on STN: 19971024
Entered Medline: 19971015

L3 ANSWER 4 OF 6 MEDLINE on STN
TI Preparation of intermediate-purity factor VIII concentrate by direct gel filtration of cryoprecipitate.
AB We report a new method to produce a solvent/detergent-treated and severe dry heat-treated factor VIII (FVIII) concentrate (3-6 IU FVIII:C/mg protein). This method, which uses a single purification step after cryoprecipitation, is suitable for scale-up to production levels. FVIII was obtained from solvent/detergent-treated cryoprecipitate by a single gel filtration step using Sephacryl S-400HR. The freeze-dried product was stable to **heating** at 80 degrees C for 72 h. The yield of the solvent/detergent and severe dry heat-treated product was 230 IU FVIII:C/kg plasma. The reconstituted product gave a 10% loss in FVIII:C activity after **heating** at 37 degrees C for 6 h. The feasibility of this method suggests that gel filtration using S-400HR can be used solely or as part of a **purification process** for the preparation of high-purity FVIII concentrates.
ACCESSION NUMBER: 94144160 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8310677
TITLE: Preparation of intermediate-purity factor VIII concentrate

by direct gel filtration of cryoprecipitate.
AUTHOR: Teh L C
CORPORATE SOURCE: Department of Blood Products Development, Auckland Regional Blood Centre, Auckland Hospital, New Zealand.
SOURCE: Vox sanguinis, (1993) 65 (4) 251-7.
Journal code: 0413606. ISSN: 0042-9007.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 19940330
Entered Medline: 19940317

L3 ANSWER 5 OF 6 MEDLINE on STN
TI Removal of viral contaminants by monoclonal antibody purification of plasma proteins.
AB The transmittance of pathogenic viruses by the widespread administration of protein fractions such as F VIII prepared on a large scale from pooled human plasma has been of growing concern. We have now demonstrated that significant amounts of pathogenic viruses including LAV/HTLVIII may be removed by a new large scale fractionation process for the preparation of human F VIII (Monoclate) which employs immunoaffinity chromatography. Model viruses representative of different virus families and the LAV strain of HIV were added to cryoprecipitate and then the mixture was processed as for Monoclate manufacturing. Virus titers were determined at each step of the fractionation procedures. An overall reduction of at least 6 logs was obtained for the model viruses and the HIV due to the **purification process**. An added **heating** step further increased the safety margin for the product resulting in at least an overall reduction of 7-9 logs for HIV. Clinical experience with Monoclate in virgin hemophiliacs has confirmed its viral safety. Our laboratories are exploiting a similar strategy of immunoaffinity chromatography to ensure the viral safety of FIX and protein C preparations derived from plasma.
ACCESSION NUMBER: 89090586 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2491983
TITLE: Removal of viral contaminants by monoclonal antibody purification of plasma proteins.
AUTHOR: Schreiber A B; Hrinda M E; Newman J; Tarr G C; D'Alisa R; Curry W M
CORPORATE SOURCE: Rorer Biotechnology Inc., King of Prussia, Pa.
SOURCE: Current studies in hematology and blood transfusion, (1989) (56) 146-53.
Journal code: 8600673. ISSN: 0258-0330.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19890223

L3 ANSWER 6 OF 6 MEDLINE on STN
TI Purification and characterization of a peptidoglycan-associated lipoprotein from Haemophilus influenzae.
AB We have purified to homogeneity a peptidoglycan-associated protein from Haemophilus influenzae. Our **purification process** used differential extraction of cell envelopes with nondenaturing detergents. Solubilization of this protein was accomplished by **heating** a peptidoglycan-enriched subcellular fraction in the presence of one of several nondenaturing detergents at 55-60 degrees C. The purified protein

migrated as a single band, with a Mr approximately 15,000, following sodium dodecyl sulfate-polyacrylamide gel electrophoresis. This protein contains covalently linked fatty acids, is rich in tyrosine, but lacks methionine and tryptophan. Amino acid analysis also revealed the presence of glycerylcysteine, which has been shown to be the site of fatty acylation in other bacterial lipoproteins. Over 87% of the primary structure has been determined by sequencing high pressure liquid chromatography purified fragments derived from several endoproteinase digests. This protein belongs to a family of proteins, known as peptidoglycan associated lipoproteins, which appear to be components of the outer membranes of most Gram-negative bacteria.

ACCESSION NUMBER: 88257108 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3290214
TITLE: Purification and characterization of a peptidoglycan-associated lipoprotein from Haemophilus influenzae.
AUTHOR: Zlotnick G W; Sanfilippo V T; Mattler J A; Kirkley D H; Boykins R A; Seid R C Jr
CORPORATE SOURCE: Department of Protein Chemistry, Praxis Biologics, Inc., Rochester, New York 14623.
SOURCE: Journal of biological chemistry, (1988 Jul 15) 263 (20) 9790-4.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198808
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 20000303
Entered Medline: 19880808

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                   alerts (SDIs) affected
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                   alerts (SDIs) affected
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                   (ROSPATENT) added to list of core patent offices covered
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               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 13:08:30 ON 02 MAR 2005

 FILE LAST UPDATED: 1 MAR 2005 (20050301/UP).  FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

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    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2005 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s purification process
        547103 PURIFICATION
        380846 PROCESS
L1         549 PURIFICATION PROCESS
               (PURIFICATION(W)PROCESS)

=> s l1 and (heating and cooling steps)
         19691 HEATING
         13883 COOLING
         63432 STEPS
            12 COOLING STEPS
               (COOLING(W)STEPS)
L2           0 L1 AND (HEATING AND COOLING STEPS)

=> s l1 and (heating)
         19691 HEATING
L3           6 L1 AND (HEATING)

=> s l3 and cooling
         13883 COOLING
L4           0 L3 AND COOLING

=> s l1 and cooling
         13883 COOLING
L5           1 L1 AND COOLING

=> d l5 ti abs ibib tot

L5   ANSWER 1 OF 1     MEDLINE on STN
TI   Comparison of purification procedures for the isolation and detection of
     anabolic residues in faeces using gas chromatography-mass spectrometry.
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AB Within several regional field laboratories and the national reference laboratory a harmonised methodology for the analysis of anabolic residues in faecal samples was developed. The method consists of a liquid-liquid and a solid-phase extraction step, followed by a high-performance liquid chromatography purification step. Using gas chromatography-mass spectrometry, currently illegally used anabolic steroids can be detected in faeces at the ppb level. Within this context acidification, followed by centrifugation under **cooling**, allows efficient, practical and rapid defatting of faecal samples. Furthermore, a combination of a silica and an aminopropyl solid-phase extraction column was found to give the best results as regards the sample **purification process**

ACCESSION NUMBER: 1999364169 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10435311
TITLE: Comparison of purification procedures for the isolation and detection of anabolic residues in faeces using gas chromatography-mass spectrometry.
AUTHOR: Hamoir T; Courtheyn D; De Brabander H; Delahaut P; Leyssens L; Pottie G
CORPORATE SOURCE: Institute of Public Health, Brussels, Belgium.
SOURCE: Analyst, (1998 Dec) 123 (12) 2621-4.
Journal code: 0372652. ISSN: 0003-2654.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990909

=> d his

(FILE 'HOME' ENTERED AT 13:07:58 ON 02 MAR 2005)

FILE 'MEDLINE' ENTERED AT 13:08:30 ON 02 MAR 2005
L1 549 S PURIFICATION PROCESS
L2 0 S L1 AND (HEATING AND COOLING STEPS)
L3 6 S L1 AND (HEATING)
L4 0 S L3 AND COOLING
L5 1 S L1 AND COOLING

=> d l6 ti abs ibib tot
L6 NOT FOUND
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=> d l3 ti abs ibib tot

L3 ANSWER 1 OF 6 MEDLINE on STN
TI The safety of fibrin sealants.
AB Fibrin sealants are prepared from fibrinogen, thrombin and sometimes also factor XIII that have been purified from human plasma. Bovine aprotinin is also included in some preparations. Each of these components has the potential to carry blood-borne pathogens, albeit at a very low frequency. In order to minimize the risk of viral transmission from commercial fibrin sealants, plasma donations undergo a series of procedures that contribute to avoiding, inactivating and eliminating potential contaminants. The procedures for selection and screening of plasma donors, and the testing of donated plasma, incorporates highly sensitive molecular techniques (e.g. PCR testing) and contributes significantly to reducing the theoretical possibility of viral transmission. The starting material for

bovine aprotinin is also carefully selected, and the manufacturing process rigorously assessed, to minimize the putative risk of transmission of bovine spongiform encephalopathies. The manufacturing process for commercial fibrin sealants comprises a range of procedures, including heat treatment (e.g. pasteurization, dry or vapor **heating**), filtration, solvent/detergent treatment, precipitation, pH treatment and chromatography. Some steps are an inherent part of the **purification process** and others (e.g. pasteurization, nanofiltration) are deliberately introduced to inactivate/eliminate potential pathogens. Current manufacturing processes provide a very high degree of safety for fibrin sealants. In 20 years of worldwide use, there have been no known cases of hepatitis or HIV transmission associated with the use of commercial fibrin sealants.

ACCESSION NUMBER: 2003337011 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12869985
TITLE: The safety of fibrin sealants.
AUTHOR: Joch Christine
CORPORATE SOURCE: Global Drug Surveillance, Aventis Behring GmbH, PO Box 1230, D-35002 Marburg, Germany.. christine.joch@aventis.com
SOURCE: Cardiovascular surgery (London, England), (2003 Aug) 11 Suppl 1 23-8.
Journal code: 9308765. ISSN: 0967-2109.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20030719
Last Updated on STN: 20031218
Entered Medline: 20031120

L3 ANSWER 2 OF 6 MEDLINE on STN
TI Strategies to avoid virus transmissions by biopharmaceutic products.
AB The use of biopharmaceutical products offers an opportunity for the treatment of many diseases. Biotechnical manufacturing using recombinant mammalian cell lines is the most appropriate method today for the production of biopharmaceutical protein drugs for the treatment of human and animal diseases. However, mammalian cell line derived products have a potential risk for virus transmission to patients who are treated with these biopharmaceutical products. The reliability that biological products are free of any viruses requires a combination of several strategies: The use of well-characterized cell bank systems and, if feasible, the avoidance of biological raw materials for the cultivation of these mammalian cell lines and the production of biopharmaceuticals. Further on, the **purification process** for biopharmaceuticals has to be validated for its ability to efficiently remove and inactivate any potential virus contamination and, where applicable, also unconventional transmissible agents, such as BSE. In addition, the biopharmaceutical product itself can be tested for the presence of viruses. Like other manufacturing processes, biotechnical production processes have to be performed in compliance with current Good Manufacturing Practices (cGMP).

ACCESSION NUMBER: 1998075464 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9413543
TITLE: Strategies to avoid virus transmissions by biopharmaceutic products.
AUTHOR: Werz W; Hoffmann H; Haberer K; Walter J K
CORPORATE SOURCE: Dr. Karl Thomae GmbH, Boehringer Ingelheim, Department of Biotech Production, Biberach/Riss, Federal Republic of Germany.
SOURCE: Archives of virology. Supplementum, (1997) 13 245-56.
Journal code: 9214275. ISSN: 0939-1983.
PUB. COUNTRY: Austria
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980126

L3 ANSWER 3 OF 6 MEDLINE on STN
TI Production, purification and characterization of Bacillus lipase.
AB The lipolytic activities in the supernatant fractions of Bacillus cereus and Bacillus coagulans cultures were investigated. Aeration, agitation, different media, emulsified oils, inoculum size and phase of growth affected lipase production. Aeration was essential for lipase production (air: medium ration 4:1) and produced the highest activity. The lipolytic activity reached a maximum level after incubation for two days with continuous agitation. It was also elevated by the presence of either olive oil or tributyrin and with lesser extent in the presence of castor oil. The enzyme levels were drastically reduced in the presence of animal fat, cotton seed oil, margarine or glycerol. The extracellular lipase enzyme from Bacillus cereus was purified with 46.2% overall recovery thought too steps, an acetone precipitation of the whole supernatant and purification by gel filtration on sephadex G-100. The efficiency of the **purification process** was evaluated through the polyacrylamide gel electrophoresis. The enzyme has an optimum pH 7.5 at the optimum incubation temperature of 40 degrees C. It is stable and retains its full activity after **heating** at 40-50 degrees C for 30 min. The activity is lost completely at 80 degrees C.
ACCESSION NUMBER: 97410479 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9265771
TITLE: Production, purification and characterization of Bacillus lipase.
AUTHOR: el-Shafei H A; Rezkallah L A
CORPORATE SOURCE: Microbial Chemistry Department, National Research Centre, Dokki, Cairo, Egypt.
SOURCE: Microbiological research, (1997 Jul) 152 (2) 199-208. Journal code: 9437794. ISSN: 0944-5013.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971024
Last Updated on STN: 19971024
Entered Medline: 19971015

L3 ANSWER 4 OF 6 MEDLINE on STN
TI Preparation of intermediate-purity factor VIII concentrate by direct gel filtration of cryoprecipitate.
AB We report a new method to produce a solvent/detergent-treated and severe dry heat-treated factor VIII (FVIII) concentrate (3-6 IU FVIII:C/mg protein). This method, which uses a single purification step after cryoprecipitation, is suitable for scale-up to production levels. FVIII was obtained from solvent/detergent-treated cryoprecipitate by a single gel filtration step using Sephacryl S-400HR. The freeze-dried product was stable to **heating** at 80 degrees C for 72 h. The yield of the solvent/detergent and severe dry heat-treated product was 230 IU FVIII:C/kg plasma. The reconstituted product gave a 10% loss in FVIII:C activity after **heating** at 37 degrees C for 6 h. The feasibility of this method suggests that gel filtration using S-400HR can be used solely or as part of a **purification process** for the preparation of high-purity FVIII concentrates.
ACCESSION NUMBER: 94144160 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8310677
TITLE: Preparation of intermediate-purity factor VIII concentrate

by direct gel filtration of cryoprecipitate.
AUTHOR: Teh L C
CORPORATE SOURCE: Department of Blood Products Development, Auckland Regional Blood Centre, Auckland Hospital, New Zealand.
SOURCE: Vox sanguinis, (1993) 65 (4) 251-7.
Journal code: 0413606. ISSN: 0042-9007.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 19940330
Entered Medline: 19940317

L3 ANSWER 5 OF 6 MEDLINE on STN
TI Removal of viral contaminants by monoclonal antibody purification of plasma proteins.
AB The transmittance of pathogenic viruses by the widespread administration of protein fractions such as F VIII prepared on a large scale from pooled human plasma has been of growing concern. We have now demonstrated that significant amounts of pathogenic viruses including LAV/HTLVIII may be removed by a new large scale fractionation process for the preparation of human F VIII (Monoclate) which employs immunoaffinity chromatography. Model viruses representative of different virus families and the LAV strain of HIV were added to cryoprecipitate and then the mixture was processed as for Monoclate manufacturing. Virus titers were determined at each step of the fractionation procedures. An overall reduction of at least 6 logs was obtained for the model viruses and the HIV due to the **purification process**. An added **heating** step further increased the safety margin for the product resulting in at least an overall reduction of 7-9 logs for HIV. Clinical experience with Monoclate in virgin hemophiliacs has confirmed its viral safety. Our laboratories are exploiting a similar strategy of immunoaffinity chromatography to ensure the viral safety of FIX and protein C preparations derived from plasma.
ACCESSION NUMBER: 89090586 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2491983
TITLE: Removal of viral contaminants by monoclonal antibody purification of plasma proteins.
AUTHOR: Schreiber A B; Hrinda M E; Newman J; Tarr G C; D'Alisa R; Curry W M
CORPORATE SOURCE: Rorer Biotechnology Inc., King of Prussia, Pa.
SOURCE: Current studies in hematology and blood transfusion, (1989) (56) 146-53.
Journal code: 8600673. ISSN: 0258-0330.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19890223

L3 ANSWER 6 OF 6 MEDLINE on STN
TI Purification and characterization of a peptidoglycan-associated lipoprotein from Haemophilus influenzae.
AB We have purified to homogeneity a peptidoglycan-associated protein from Haemophilus influenzae. Our **purification process** used differential extraction of cell envelopes with nondenaturing detergents. Solubilization of this protein was accomplished by **heating** a peptidoglycan-enriched subcellular fraction in the presence of one of several nondenaturing detergents at 55-60 degrees C. The purified protein

migrated as a single band, with a Mr approximately 15,000, following sodium dodecyl sulfate-polyacrylamide gel electrophoresis. This protein contains covalently linked fatty acids, is rich in tyrosine, but lacks methionine and tryptophan. Amino acid analysis also revealed the presence of glycerylcysteine, which has been shown to be the site of fatty acylation in other bacterial lipoproteins. Over 87% of the primary structure has been determined by sequencing high pressure liquid chromatography purified fragments derived from several endoproteinase digests. This protein belongs to a family of proteins, known as peptidoglycan associated lipoproteins, which appear to be components of the outer membranes of most Gram-negative bacteria.

ACCESSION NUMBER: 88257108 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3290214
TITLE: Purification and characterization of a peptidoglycan-associated lipoprotein from Haemophilus influenzae.
AUTHOR: Zlotnick G W; Sanfilippo V T; Mattler J A; Kirkley D H; Boykins R A; Seid R C Jr
CORPORATE SOURCE: Department of Protein Chemistry, Praxis Biologics, Inc., Rochester, New York 14623.
SOURCE: Journal of biological chemistry, (1988 Jul 15) 263 (20) 9790-4.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198808
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 20000303
Entered Medline: 19880808

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L2 0 S L1 AND (HEATING AND COOLING STEPS)
L3 6 S L1 AND (HEATING)
L4 0 S L3 AND COOLING
L5 1 S L1 AND COOLING

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43149 SUGAR
L6 7 L1 AND SUGAR

=> s l6 and heating
19691 HEATING
L7 0 L6 AND HEATING

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                   National Meeting on March 13, 2005
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               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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FULL ESTIMATED COST                                       0.21       0.21

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=> s insulin analog
L1          737 INSULIN ANALOG

=> s l1 and insulin precursor
L2           44 L1 AND INSULIN PRECURSOR

=> s protein purification
L3        46617 PROTEIN PURIFICATION

=> s l3 and l2
L4            2 L3 AND L2

=> d l4 ti abs ibib ott
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FP --------- PI, TI, IN, INA, PA, PAA, PAT, PTERM, DCD, AI, RLI,
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              NCLM, NCLS, EXF, REP, REN, ARTU, EXNAM, LREP,
              CLMN, DRWN, AB
FP.EX ------ FP for original and latest publication
FPALL ------ PI, TI, IN, INA, PA, PAA, PAT, PETRM, DCD, AI,
              RLI, PRAI, IC, ICM, ICS, INCL, INCLM, INCLS, NCL, NCLM,
              NCLS, EXF, REP, REN,ARTU, EXNAM, LREP, CLMN, DRWN, AB,
              PARN, SUMM, DRWD, DETD, CLM
FPBIB ------ PI, TI, IN, INA, PA, PAA, PAT, PTERM, DCD, AI,
              RLI, PRAI, REP, REN, EXNAM, LREP, CLM, CLMN, DRWN
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HITSTR ----- HIT RN, its text modification, its CA index name, and
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IBIBG ------ IBIB plus PAGE.DRAW
IMAX -------- MAX, indented with text labels
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IND -------- INCL, INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,
              EXF, ARTU, OS, CC, SX, ST, IT
ISTD ------- STD, indented with text labels
KWIC ------- All hit terms plus 20 words on either side
MAX -------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PTERM, DCD,
              RLI, PRAI, DT, FS, REP, REN, EXNAM, LREP, CLMN, ECL,
              DRWN, AB, GOVI, PARN, SUMM, DRWD, DETD, CLM, INCL,
              INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,
              EXF, ARTU OS, CC, SX, ST, IT
MAX.EX ----- MAX for original and latest publication
OCC -------- List of display fields containing hit terms
SBIB ------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, RLI, PRAI,
              DT, FS, LN.CNT
SCAN ------- AN, TI, NCL, NCLM, NCLS, IC, ICM, ICS (random display
              without answer number.  SCAN must be entered on the
              same line as DISPLAY, e.g., D SCAN)
STD -------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, RLI, PRAI,
              DT, FS, LN.CNT, INCL, INCLM, INCLS, NCL, NCLM, NCLS,
              IC, ICM, ICS, EXF (STD is the default)
STD.EX ----- STD for original and latest publication
TRIAL ------ AN, TI, INCL, INCLM, INCLS, NCL, NCLM, NCLS, IC,
              ICM, ICS

ENTER DISPLAY FORMAT (STD):ene
'ENE' IS NOT A VALID FORMAT FOR FILE 'USPATFULL'

The following are valid formats:

The default display format is STD.

ABS -------- AB
ALL -------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PTERM, DCD,
              RLI, PRAI, DT, FS, REP, REN, EXNAM, LREP, CLMN, ECL,
              DRWN, AB, GOVI, PARN, SUMM, DRWD, DETD, CLM, INCL,
              INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,
              EXF, ARTU
ALLG ------- ALL plus PAGE.DRAW
BIB -------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PTERM, DCD, RLI,
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             PRAI, DT, FS, EXNAM, LREP, CLMN, ECL, DRWN, LN.CNT
BIB.EX ----- BIB for original and latest publication
BIBG ------- BIB plus PAGE.DRAW
BROWSE ----- See "HELP BROWSE" or "HELP DISPLAY BROWSE".  BROWSE must
             entered on the same line as DISPLAY, e.g., D BROWSE.
CAS -------- OS, CC, SX, ST, IT
CBIB ------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PRAI, DT, FS
DALL ------- ALL, delimited for post-processing
FP --------- PI, TI, IN, INA, PA, PAA, PAT, PTERM, DCD, AI, RLI,
             PRAI, IC, ICM, ICS, INCL, INCLM, INCLS, NCL,
             NCLM, NCLS, EXF, REP, REN, ARTU, EXNAM, LREP,
             CLMN, DRWN, AB
FP.EX ------ FP for original and latest publication
FPALL ------ PI, TI, IN, INA, PA, PAA, PAT, PETRM, DCD, AI,
             RLI, PRAI, IC, ICM, ICS, INCL, INCLM, INCLS, NCL, NCLM,
             NCLS, EXF, REP, REN,ARTU, EXNAM, LREP, CLMN, DRWN, AB,
             PARN, SUMM, DRWD, DETD, CLM
FPBIB ------ PI, TI, IN, INA, PA, PAA, PAT, PTERM, DCD, AI,
             RLI, PRAI, REP, REN, EXNAM, LREP, CLM, CLMN, DRWN
FHITSTR ---- HIT RN, its text modification, its CA index name, and
             its structure diagram
FPG -------- FP plus PAGE.DRAW
GI --------- PN and page image numbers
HIT -------- All fields containing hit terms
HITRN ------ HIT RN and its text modification
HITSTR ----- HIT RN, its text modification, its CA index name, and
             its structure diagram
IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IALLG ------ IALL plus PAGE.DRAW
IBIB ------- BIB, indented with text labels
IBIB.EX ---- IBIB for original and latest publication
IBIBG ------ IBIB plus PAGE.DRAW
IMAX ------- MAX, indented with text labels
IMAX.EX ---- IMAX for original and latest publication
IND -------- INCL, INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,
             EXF, ARTU, OS, CC, SX, ST, IT
ISTD ------- STD, indented with text labels
KWIC ------- All hit terms plus 20 words on either side
MAX -------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PTERM, DCD,
             RLI, PRAI, DT, FS, REP, REN, EXNAM, LREP, CLMN, ECL,
             DRWN, AB, GOVI, PARN, SUMM, DRWD, DETD, CLM, INCL,
             INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,
             EXF, ARTU OS, CC, SX, ST, IT
MAX.EX ----- MAX for original and latest publication
OCC -------- List of display fields containing hit terms
SBIB ------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, RLI, PRAI,
             DT, FS, LN.CNT
SCAN ------- AN, TI, NCL, NCLM, NCLS, IC, ICM, ICS (random display
             without answer number.  SCAN must be entered on the
             same line as DISPLAY, e.g., D SCAN)
STD -------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, RLI, PRAI,
             DT, FS, LN.CNT, INCL, INCLM, INCLS, NCL, NCLM, NCLS,
             IC, ICM, ICS, EXF (STD is the default)
STD.EX ----- STD for original and latest publication
TRIAL ------ AN, TI, INCL, INCLM, INCLS, NCL, NCLM, NCLS, IC,
             ICM, ICS

ENTER DISPLAY FORMAT (STD):end

=> d his

     (FILE 'HOME' ENTERED AT 13:23:56 ON 03 MAR 2005)
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FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS' ENTERED AT 13:24:15 ON 03 MAR 2005

L1 737 S INSULIN ANALOG
L2 44 S L1 AND INSULIN PRECURSOR
L3 46617 S PROTEIN PURIFICATION
L4 2 S L3 AND L2

=> d l4 ti abs ibib tot

L4 ANSWER 1 OF 2 USPATFULL on STN
TI Methods for the production of insulin in plants
AB Methods for the production of insulin in plants are described. In one embodiment, the present invention provides a method for the expression of insulin in plants comprising:

(a) providing a chimeric nucleic acid construct comprising in the 5' to 3' direction of transcription as operably linked components:

(i) a nucleic acid sequence capable of controlling expression in plant seed cells; and

(ii) a nucleic acid sequence encoding an insulin polypeptide;

(b) introducing the chimeric nucleic acid construct into a plant cell; and

(c) growing the plant cell into a mature plant capable of setting seed wherein the seed expresses insulin.

ACCESSION NUMBER:	2005:45499 USPATFULL		
TITLE:	Methods for the production of insulin in plants		
INVENTOR(S):	Moloney, Maurice M., Calgary, CANADA Boothe, Joseph, Calgary, CANADA Keon, Richard, Calgary, CANADA Nykiforuk, Cory, Calgary, CANADA Van Rooijen, Gijs, Calgary, CANADA		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005039235	A1	20050217
APPLICATION INFO.:	US 2004-869040	A1	20040617 (10)
	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-478818P	20030617 (60)	
	US 2004-549539P	20040304 (60)	
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	BERESKIN AND PARR, SCOTIA PLAZA, 40 KING STREET WEST-SUITE 4000 BOX 401, TORONTO, ON, M5H 3Y2		
NUMBER OF CLAIMS:	40		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	17 Drawing Page(s)		
LINE COUNT:	4386		

L4 ANSWER 2 OF 2 USPATFULL on STN
TI Proteins with insulin-like activity useful in the treatment of diabetes
AB The invention relates to novel insulin activity (IA) proteins and nucleic acids. The Invention further relates to the use of the IA proteins in the treatment of insulin related disorders such as type 1 diabetes and type 2 diabetes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2004:141132 USPATFULL

TITLE: Proteins with insulin-like activity useful in the treatment of diabetes
INVENTOR(S): Dahiyat, Bassil I., Los Angeles, CA, United States
Morton, Andrew G., late of Mt. Lebanon, PA, United States deceased
Bassil I. Dahiyat, United States legal representative
PATENT ASSIGNEE(S): Xencor, Inc., Monrovia, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6746853	B1	20040608
APPLICATION INFO.:	US 2000-574443		20000519 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-134930P	19990519 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Saoud, Christine J.
LEGAL REPRESENTATIVE: Dorsey & Whitney LLP, Silva, Robin M., Kosslak, Renee M.
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1,14
NUMBER OF DRAWINGS: 28 Drawing Figure(s); 10 Drawing Page(s)
LINE COUNT: 4012
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 13:23:56 ON 03 MAR 2005)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS' ENTERED AT 13:24:15 ON 03 MAR 2005
L1 737 S INSULIN ANALOG
L2 44 S L1 AND INSULIN PRECURSOR
L3 46617 S PROTEIN PURIFICATION
L4 2 S L3 AND L2

=> d l2 ti abs ibib 1-10

L2 ANSWER 1 OF 44 USPATFULL on STN
TI Methods for the production of insulin in plants
AB Methods for the production of insulin in plants are described. In one embodiment, the present invention provides a method for the expression of insulin in plants comprising:

(a) providing a chimeric nucleic acid construct comprising in the 5' to 3' direction of transcription as operably linked components:

(i) a nucleic acid sequence capable of controlling expression in plant seed cells; and

(ii) a nucleic acid sequence encoding an insulin polypeptide;

(b) introducing the chimeric nucleic acid construct into a plant cell; and

(c) growing the plant cell into a mature plant capable of setting seed wherein the seed expresses insulin.

ACCESSION NUMBER: 2005:45499 USPATFULL
TITLE: Methods for the production of insulin in plants

INVENTOR(S): Moloney, Maurice M., Calgary, CANADA
Boothe, Joseph, Calgary, CANADA
Keon, Richard, Calgary, CANADA
Nykiforuk, Cory, Calgary, CANADA
Van Rooijen, Gijs, Calgary, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005039235	A1	20050217	
APPLICATION INFO.:	US 2004-869040	A1	20040617	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-478818P	20030617	(60)
	US 2004-549539P	20040304	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BERESKIN AND PARR, SCOTIA PLAZA, 40 KING STREET WEST-SUITE 4000 BOX 401, TORONTO, ON, M5H 3Y2
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Page(s)
LINE COUNT: 4386

L2 ANSWER 2 OF 44 USPATFULL on STN
TI Insulin molecule having protracted time action
AB The present invention provides an insulin molecule that provides a protracted, even basal duration of action. The insulin molecule comprises a modification at the N-terminus of the A-chain, optionally a modification at the N-terminus of the B-chain, a modification at a B-chain lysine, and optionally a modification at the C-terminus of the A-chain. The present invention also provides a method of treating diabetes mellitus comprising administering the insulin molecule.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2005:17277 USPATFULL
TITLE: Insulin molecule having protracted time action
INVENTOR(S): Beals, John Michael, Indianapolis, IN, UNITED STATES
DeFelippis, Michael Rosario, Carmel, IN, UNITED STATES
DiMarchi, Richard Dennis, Carmel, IN, UNITED STATES
Kohn, Wayne David, Indianapolis, IN, UNITED STATES
Micanovic, Radmila, Indianapolis, IN, UNITED STATES
Myers, Sharon Ruth, Indianapolis, IN, UNITED STATES
Ng, Kingman, Carmel, IN, UNITED STATES
Zhang, Lianshan, Carmel, IN, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005014679	A1	20050120	
APPLICATION INFO.:	US 2004-496847	A1	20040525	(10)
	WO 2002-US37601		20021212	

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-344310P	20011220	(60)
	US 2002-414604P	20020927	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ELI LILLY AND COMPANY, PATENT DIVISION, P.O. BOX 6288, INDIANAPOLIS, IN, 46206-6288
NUMBER OF CLAIMS: 53
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 3153

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 3 OF 44 USPATFULL on STN
TI Purification process comprising microfiltration at elevated temperatures
AB Process for microfiltration at elevated temperature.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2004:212922 USPATFULL			
TITLE:	Purification process comprising microfiltration at elevated temperatures			
INVENTOR(S):	Christensen, Lars Hojlund, Vaerlose, DENMARK Nielsen, Torben Kjaersgaard, Roskilde, DENMARK			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004164023	A1	20040826	
APPLICATION INFO.:	US 2003-671064	A1	20030925	(10)
	NUMBER		DATE	
PRIORITY INFORMATION:	DK 2002-1422		20020925	
	US 2002-413729P		20020926	(60)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	NOVO NORDISK PHARMACEUTICALS, INC, 100 COLLEGE ROAD WEST, PRINCETON, NY, 08540			
NUMBER OF CLAIMS:	34			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	2 Drawing Page(s)			
LINE COUNT:	629			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 4 OF 44 USPATFULL on STN
TI Method for purifying a fermentation-derived product
AB Process for purifying a fermentation-derived product.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2004:178404 USPATFULL			
TITLE:	Method for purifying a fermentation-derived product			
INVENTOR(S):	Markussen, Jan, Herlev, DENMARK Diers, Ivan, Vaerlose, DENMARK			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004137571	A1	20040715	
APPLICATION INFO.:	US 2003-719601	A1	20031121	(10)
	NUMBER		DATE	
PRIORITY INFORMATION:	DK 2002-1821		20021126	
	US 2002-430748P		20021204	(60)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	NOVO NORDISK PHARMACEUTICALS, INC, 100 COLLEGE ROAD WEST, PRINCETON, NY, 08540			
NUMBER OF CLAIMS:	21			
EXEMPLARY CLAIM:	1			
LINE COUNT:	481			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 5 OF 44 USPATFULL on STN
TI Proteins with insulin-like activity useful in the treatment of diabetes
AB The invention relates to novel insulin activity (IA) proteins and nucleic acids. The Invention further relates to the use of the IA

proteins in the treatment of insulin related disorders such as type 1 diabetes and type 2 diabetes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2004:141132 USPATFULL			
TITLE:	Proteins with insulin-like activity useful in the treatment of diabetes			
INVENTOR(S):	Dahiyat, Bassil I., Los Angeles, CA, United States Morton, Andrew G., late of Mt. Lebanon, PA, United States deceased Bassil I. Dahiyat, United States legal representative			
PATENT ASSIGNEE(S):	Xencor, Inc., Monrovia, CA, United States (U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6746853	B1	20040608	
APPLICATION INFO.:	US 2000-574443		20000519	(9)
	NUMBER		DATE	
PRIORITY INFORMATION:	US 1999-134930P		19990519	(60)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	GRANTED			
PRIMARY EXAMINER:	Saoud, Christine J.			
LEGAL REPRESENTATIVE:	Dorsey & Whitney LLP, Silva, Robin M., Kosslak, Renee M.			
NUMBER OF CLAIMS:	14			
EXEMPLARY CLAIM:	1,14			
NUMBER OF DRAWINGS:	28 Drawing Figure(s); 10 Drawing Page(s)			
LINE COUNT:	4012			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 6 OF 44 USPATFULL on STN

TI Insulin polypeptide-oligomer conjugates, proinsulin polypeptide-oligomer conjugates and methods of synthesizing same

AB Methods for synthesizing proinsulin polypeptides are described that include contacting a proinsulin polypeptide including an insulin polypeptide coupled to one or more peptides by peptide bond(s) capable of being cleaved to yield the insulin polypeptide with an oligomer under conditions sufficient to couple the oligomer to the insulin polypeptide portion of the proinsulin polypeptide and provide a proinsulin polypeptide-oligomer conjugate, and cleaving the one or more peptides from the proinsulin polypeptide-oligomer conjugate to provide the insulin polypeptide-oligomer conjugate. Methods of synthesizing proinsulin polypeptide-oligomer conjugates are also provided as are proinsulin polypeptide-oligomer conjugates. Methods of synthesizing C-peptide polypeptide-oligomer conjugates and other pro-polypeptide-oligomer conjugates are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:325027 USPATFULL			
TITLE:	Insulin polypeptide-oligomer conjugates, proinsulin polypeptide-oligomer conjugates and methods of synthesizing same			
INVENTOR(S):	Soltero, Richard, Holly Springs, NC, UNITED STATES Radhakrishnan, Balasingam, Chapel Hill, NC, UNITED STATES Ekwuribe, Nnochiri N., Cary, NC, UNITED STATES			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003229009	A1	20031211	
APPLICATION INFO.:	US 2003-382022	A1	20030305	(10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-36744, filed on 21 Dec 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-318197P	20010907 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627
NUMBER OF CLAIMS: 124
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 40 Drawing Page(s)
LINE COUNT: 6219
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 7 OF 44 USPATFULL on STN
TI Insulin polypeptide-oligomer conjugates, proinsulin polypeptide-oligomer conjugates and methods of synthesizing same
AB Methods for synthesizing proinsulin polypeptides are described that include contacting a proinsulin polypeptide including an insulin polypeptide coupled to one or more peptides by peptide bond(s) capable of being cleaved to yield the insulin polypeptide with an oligomer under conditions sufficient to couple the oligomer to the insulin polypeptide portion of the proinsulin polypeptide and provide a proinsulin polypeptide-oligomer conjugate, and cleaving the one or more peptides from the proinsulin polypeptide-oligomer conjugate to provide the insulin polypeptide-oligomer conjugate. Methods of synthesizing proinsulin polypeptide-oligomer conjugates are also provided as are proinsulin polypeptide-oligomer conjugates. Methods of synthesizing C-peptide polypeptide-oligomer conjugates and other pro-polypeptide-oligomer conjugates are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:324677 USPATFULL
TITLE: Insulin polypeptide-oligomer conjugates, proinsulin polypeptide-oligomer conjugates and methods of synthesizing same
INVENTOR(S): Radhakrishnan, Balasingam, Chapel Hill, NC, UNITED STATES
Soltero, Richard, Holly Springs, NC, UNITED STATES
Ekwuribe, Nnochiri N., Cary, NC, UNITED STATES
Puskas, Monica, Spring Hope, NC, UNITED STATES
Sangal, Diti, Morrisville, NC, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003228652	A1	20031211
APPLICATION INFO.:	US 2003-389499	A1	20030317 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-382022, filed on 5 Mar 2003, PENDING Continuation-in-part of Ser. No. US 2001-36744, filed on 21 Dec 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-318197P	20010907 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627
NUMBER OF CLAIMS: 142
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 40 Drawing Page(s)
LINE COUNT: 6285

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 8 OF 44 USPATFULL on STN
TI Method for making insulin precursors and **insulin precursor** analogs
AB Novel insulin precursors and **insulin precursor** analogs having a mini C-peptide comprising at least one aromatic amino acid residue have an increased folding stability. The novel insulin precursors and **insulin precursor** analogs can be expressed in yeast in high yields and are preferably not more 15 amino acid residues in length. Also provided are polynucleotide sequences encoding the claimed precursors or precursor analogs, and vectors and cell lines containing such polynucleotide sequences.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:271669 USPATFULL		
TITLE:	Method for making insulin precursors and **insulin precursor** analogs		
INVENTOR(S):	Kjeldsen, Thomas Borglum, Virum, DENMARK Ludvigsen, Svend, Lynge, DENMARK Kaarsholm, Niels C., Vanlose, DENMARK		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003191277	A1	20031009
APPLICATION INFO.:	US 2002-316421	A1	20021211 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-736611, filed on 14 Dec 2000, GRANTED, Pat. No. US 6521738		
	NUMBER	DATE	
PRIORITY INFORMATION:	DK 1999-1868	19991229	
	DK 2000-440	20000317	
	US 2000-181443P	20000210 (60)	
	US 2000-211441P	20000613 (60)	
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Reza Green, Esq., Novo Nordisk Pharmaceuticals, Inc., 100 College Road West, Princeton, NJ, 08540		
NUMBER OF CLAIMS:	94		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	9 Drawing Page(s)		
LINE COUNT:	2836		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 9 OF 44 USPATFULL on STN
TI Method for making insulin precursors and **insulin analog** precursors
AB Novel insulin precursors and insulin analogue precursors comprising a connecting C-peptide and an N-terminal extension are easy to handle in down stream processing and are expressed in high yields. The precursors are characterized in that the connecting peptide, the N-terminal extension or both contain at least one glycosylation site.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:58034 USPATFULL		
TITLE:	Method for making insulin precursors and **insulin analog** precursors		
INVENTOR(S):	Diers, Ivan, Vaerlose, DENMARK Kjeldsen, Thomas, Virum, DENMARK		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003040601	A1	20030227

APPLICATION INFO.: US 2002-166241 A1 20020607 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	DK 2001-894	20010608
	US 2001-299091P	20010618 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: NOVO NORDISK OF NORTH AMERICA, INC, 405 LEXINGTON AVENUE, SUITE 6400, NEW YORK, NY, 10017
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
LINE COUNT: 762
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 10 OF 44 USPATFULL on STN
TI Method for making insulin precursors and **insulin precursor** analogues having improved fermentation yield in yeast
AB Novel insulin precursors and **insulin precursor** analogs comprising a connecting peptide (mini C-peptide) of preferably up to 15 amino acid residues and comprising at least one Gly are provided. The precursors can be converted into human insulin or a human **insulin analog**. The precursors will typically have a distance between B27 (atom CG2) and A1 (atom CA) of less than 5 Å.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2002:251199 USPATFULL
TITLE: Method for making insulin precursors and **insulin precursor** analogues having improved fermentation yield in yeast
INVENTOR(S): Kjeldsen, Thomas Borglum, Virum, DENMARK
Ludvigsen, Svend, Lynge, DENMARK

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002137144	A1	20020926
	US 6777207	B2	20040817
APPLICATION INFO.:	US 2001-894711	A1	20010628 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-740359, filed on 19 Dec 2000, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	DK 1999-1869	19991229
	DK 2000-443	20000317
	US 2000-181450P	20000210 (60)
	US 2000-211081P	20000613 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Reza Green, Esq., Novo Nordisk of North America, Inc., Suite 6400, 405 Lexington Avenue, New York, NY, 10174-6401
NUMBER OF CLAIMS: 72
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Page(s)
LINE COUNT: 2550
CAS INDEXING IS AVAILABLE FOR THIS PATENT.